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ROSACEA KERATITIS AND CONDITIONS WITH VASCULARIZATION OF CORNEA TREATED WITH RIBOFLAVIN

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In a previous communication observations on the corneas of rats whose diet was deficient in riboflavin (vitamin B_2) were recorded. At that time we said: "From our experience with the diet deficient in riboflavin, the most consistent ocular change was the appearance of corneal vascularization. . . . After riboflavin was added, the most uniform effect was remission of vascularization." [1] While the article was in press, a similar opinion was expressed by Bessey and Wolbach: [2] "Vascularization of the cornea is an early and constant phenomenon in albino rats in riboflavin deficiency. It precedes all other demonstrable lesions of the deficiency." Conspicuous cutaneous features are intense flushing of the skin and alopecia.

A chemical and pharmacologic description of riboflavin follows:

Riboflavin is the name which was proposed by the Council on Pharmacy and Chemistry of the American Medical Association [3] for the compound 6,7-dimethyl-9-(d,l'-ribityl)-isoalloxazin, which has the structure shown in figure 1.

This compound is an intensely yellow, water-soluble pigment which exhibits a distinct green fluorescence under ultraviolet rays. It has been isolated from milk,[4]

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1. Eckardt, R. E., and Johnson, L. V.: Nutritional Cataract and Relation of Galactose to Appearance of Senile Suture Line in Rats, Arch. Ophth. **21**:315 (Feb.) 1939.

2. Bessey, O. A., and Wolbach, S. B.: Vascularization of the Cornea of the Rat in Riboflavin Deficiency, with a Note on Corneal Vascularization in Vitamin A Deficiency, J. Exper. Med. **69**:1 (Jan.) 1939.

3. Riboflavin, the Accepted Name for Vitamin B_2, Report of the Council on Pharmacy and Chemistry, J. A. M. A. **108**:1340 (April 17) 1937.

4. Kuhn, R.; Rudy, H., and Wagner-Jauregg, T.: Ueber Lactoflavin (Vitamin B_2), Ber. d. deutsch. chem. Gesellsch. **66**:1950 (Dec.) 1933.

liver,[5] egg white [6] and many other foods. Its growth-promoting activity for rats has been known for a long time.[7] Riboflavin is destroyed by visible light and by ultraviolet rays in both alkaline and acid solutions.

As a result of the work of Warburg and Christian, and others [8] it is now believed that practically all, if not absolutely all, animal cells contain an enzyme which is used in the oxidation of carbohydrate by the cell. This enzyme has been known as "Warburg's yellow enzyme." Kuhn and Rudy,[9] as a result of their investigations into the phosphoric acid ester of riboflavin and its synthesis into the yellow enzyme, have proposed a structure for the yellow enzyme which is as shown in figure 2.

The more recent investigations on oxidative enzymes which contain riboflavin indicate that there exists, in addition to the yellow enzyme, which acts as a hydrogen acceptor in oxidation of carbohydrate, yet other riboflavin-protein com-

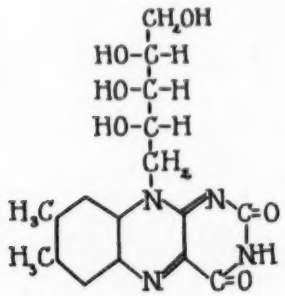

Figure 1

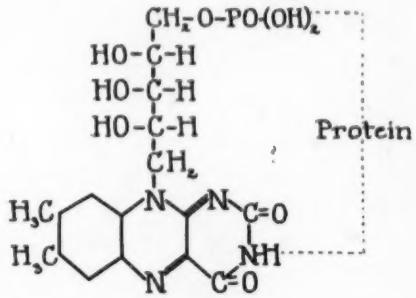

Figure 2

Fig. 1.—Riboflavin.

Fig. 2.—Warburg's yellow enzyme.

plexes which act as activators of the reduced coenzyme. Thus, Corran and Green [10] have isolated from milk a riboflavin-protein compound which catalyzes the oxida-

5. Karrer, P.; Sälomon, H., and Schopp, K.: Isolierung des Hepaflavins, Helvet. chim. acta **17**:419 (March) 1934.

6. Kuhn, R.; György, P., and Wagner-Jauregg, T.: Ueber Ovoflavin, den Farbstoff des Eiklars, Ber. d. deutsch. chem. Gesellsch. **66**:576 (April) 1933.

7. György, P.; Kuhn, R., and Wagner-Jauregg, T.: Das Vitamin B_2, Naturwissenschaften **21**:560, 1933.

8. Warburg, O., and Christian, W.: Ueber ein neues Oxydationsferment und sein Absorptionsspektrum, Biochem. Ztschr. **254**:438 (Oct.) 1932; Ueber das neue Oxydationsferment, Naturwissenschaften **20**:980, 1932. Theorell, H.: Reindarstellung (Kristallisation) des gelben Atmungsferment und die reversible Spaltung desselben, Biochem. Ztschr. **272**:155 (July) 1934; Ueber die Wirkungsgruppe des gelben Ferments, ibid. **275**:37 (Dec.) 1934; Reindarstellung der Wirkungsgruppe des gelben Ferments, ibid. **275**:344 (Jan.) 1935. Kuhn and Rudy.[9] Kuhn, R.; Rudy, H., and Weygand, F.: Ueber die Bildung eines künstlichen Ferments aus 6,7-Dimethyl-9-1-Araboflavin-5'-Phosphorsaüre, Ber. d. deutsch. chem. Gesellsch. **69**:2034 (Sept.) 1936.

9. Kuhn, R., and Rudy, H.: Katalytische Wirkung der Lactoflavin -5'- Phosphosäure; Synthese des gelben Ferments, Ber. d. deutsch. chem. Gesellsch. **69**: 1974 (Aug.) 1936.

10. Corran, H. S., and Green, D. E.: Isolation of a Flavin-Protein Compound from Milk, Nature, London (supp.) **142**:149 (July 23) 1938.

tion of reduced coenzyme by hydrogen carriers, such as methylthionine chloride (methylene blue) and riboflavin phosphoric acid ester, while Straub[11] has discovered a similar complex in heart muscle. In the light of these investigations, the older concepts of oxidation reactions must now be altered and may be expressed as follows:

substrate + dehydrogenase → activated substrate
activated substrate + coenzyme I → oxidized substrate + reduced coenzyme I
reduced coenzyme I + newer flavoproteins → activated reduced coenzyme I
activated reduced coenzyme + hydrogen acceptor[12] → coenzyme I + reduced hydrogen acceptor

The flavoproteins more recently isolated seem to act catalytically not only in the oxidation of carbohydrates (hexose and triose monophosphoric acid esters) but in the oxidation of amino acids. Another riboflavin-containing enzyme which is concerned in the oxidation of amino acids is a combination of riboflavin phosphoric acid ester and adenine. The end results, however, of riboflavin deficiency would not be affected by these newer concepts, for such a deficiency would result in a severe disturbance to the oxidative systems in the body.

From the preceding considerations, it can be seen that the function of the yellow enzyme is to aid in the transfer of hydrogen from the tissue cells to the blood stream, where free oxygen is available from the breakdown of oxyhemoglobin to hemoglobin and where the oxidation of the hydrogen received originally from the substrate, through the coenzyme, can be accomplished. It should be remembered that oxidation does not consist alone of the addition of oxygen to a compound but may be accomplished also by the removal of hydrogen from a compound. This may be represented schematically as the reaction for the oxidation of ethyl alcohol, thus:

$$CH_3CH_2OH - 2H \rightarrow CH_3CHO$$

After being activated by the dehydrogenase, then the substrate itself becomes oxidized by giving up hydrogen to the coenzyme. The enzymatic nature of the yellow enzyme is indicated by the fact that it is reversibly reduced by the coenzyme, becoming reoxidized, without change, in the presence of molecular oxygen.

The need for riboflavin in the diet is believed to be due to the fact that it is an essential constituent of the oxidation system of the yellow enzyme. Since the cells are incapable of synthesizing the riboflavin, it must be continually supplied from exogenous sources, to replace that lost in the urine and other excretions. Presumably the riboflavin is phosphorylated in the small intestine,[13] but phosphorylation can be accomplished after parenteral administration. The combination of the phosphoric acid ester of riboflavin with protein is probably accomplished within the cell. It is believed[14] that if hemin substances are

11. Straub, F. B.: Flavo-Protein of the Heart Muscle Tissue, Nature, London **143**:76 (Jan. 14) 1939.

12. Methylthionine chloride (methylene blue), riboflavin phosphoric acid ester and cytochrome c.

13. Rudy, H.: Enzymatische Phosphorylierung des Lactoflavins, Naturwissenschaften **23**:286 (May 3) 1935.

14. Hogan, A. G.: Riboflavin: Physiology and Pathology, J. A. M. A. **110**: 1188 (April 9) 1938.

not present in a tissue (such as the avascular cornea) the oxidation within the cell is accomplished by Warburg's yellow enzyme. This fact is of particular interest in this investigation of vascularization of the cornea.

The cornea is a completely avascular tissue, so that hemin substances are not brought into close proximity with the corneal cells. Consequently it may be assumed that the greater part of gaseous interchange in oxidation is effected through Warburg's yellow enzyme, as given in the preceding reactions. Furthermore, when there is a deficiency of riboflavin this oxidative system is seriously impaired, since the riboflavin is an important constituent of Warburg's yellow enzyme. The proliferation of capillaries from the limbus into the cornea is easily explained, therefore, as an attempt by the cornea to overcome local asphyxia by bringing available oxygen into closer proximity with the cells of the cornea. Regression of the corneal vessels on addition of riboflavin to the diet follows the restoration of Warburg's yellow enzyme system to its normal position in oxidation.

The cornea receives its nourishment by diffusion from the limbic vessels or from the aqueous humor. Oxygen is able to pass directly through the epithelium inward and carbonic acid from within outward. It may be inferred, however, that these means are not essential for the cornea from the facts that a cornea may be long covered with ointment, which prevents contact with the atmosphere, and that air in the anterior chamber may for a considerable length of time prevent contact with the aqueous humor. That fixed channels from the limbus are not essential is apparent from the healthy state following complete peritomy, large corneal sections and corneal transplantation.

We have observed, in particular, that ointment or liquid petrolatum over the cornea does not hasten vascularization in riboflavin-deficient rats which have mild and early vascularization. It would appear that deficiency of the vitamin itself, or of the oxidative enzyme which derives from it, is the major factor which produces vascularization of the corneas of rats on a diet deficient in riboflavin.

For the purpose of emphasis, it seems advisable to restate two properties of riboflavin: 1. Riboflavin is easily destroyed when the p_H is not on the acid side. 2. Riboflavin is biologically inactivated by light. It is apparent that the only natural source of riboflavin is food and that since riboflavin appears to be utilized in the form of riboflavin phosphoric acid ester, which the body appears normally to have little difficulty in forming, the requisites for an adequate supply of the vitamin would be: (1) adequate diet, (2) favorable acid p_H of the gastric contents, (3) normal ability to convert the riboflavin into riboflavin phosphoric acid ester, (4) normal absorption from the intestines and (5), as it concerns the cornea and the exposed face, possibly the prevention of inactivation by light.

In order to investigate the extent to which ordinary sunlight would biologically inactivate the oxidative enzymes of the rat cornea, alternate groups of rats which appeared to be in comparative stages of vascularization were placed in direct sunlight and in a room having ordinary illumination. Rats which manifested deficiency but did not show vascularization were also submitted to the same conditions. Sunlight hastened vascularization in both groups.

CLINICAL STUDY

The remarkable therapeutic effects of riboflavin on the vascularization of rats fed diets deficient in riboflavin, as well as the apparent inference that the mechanism in the growth of blood vessels was the result of faulty oxidation-reduction processes in the cornea, immediately suggested the therapeutic trial of riboflavin for human beings with vascularization of various types. It was early obvious that one form of vascularization of the human cornea promptly and consistently responded to the oral administration of riboflavin, namely, so-called rosacea keratitis. Some of the persons with rosacea keratitis also had cutaneous rosacea; a few had acne vulgaris, and most of them had marked telangiectasia and a conspicuous flushing of the skin.

Figures 3 to 6 show four representative patients. It can be seen that if a cutaneous condition is present in all cases of so-called rosacea keratitis, it occurs as flushing of the skin, telangiectasia and hypertrophy of the skin over the nose, brow and cheeks, such as is seen in acne vulgaris and rosacea. Seborrheic dermatitis is present in most of these cases but appears not to be influenced by treatment with riboflavin. These patients each have, to some extent, pustules which may contain Demodex.

During this study riboflavin [15] was administered in the following forms: 1. Pure crystalline natural riboflavin, each tablet containing 1 mg. This form of administration produced satisfactory results, but the cost prevented extensive use. 2. An adsorbate of natural riboflavin onto fullers' earth, each tablet containing 1 mg. of natural riboflavin. This form was almost totally ineffective, and several patients appeared definitely worse with the treatment. The ineffectiveness of this preparation may have been due to lack of elution of the riboflavin from the

15. All riboflavin was supplied by the Biochemicals Division of the S. M. A. Corporation. For practical purposes, riboflavin should be administered in adequate doses. The widely used so-called A-B-D-G pills and polytaxin both appear to us to contain too small amounts of riboflavin to be effective. In this connection one should bear in mind that 1 quart (0.9 liter) of milk contains almost 1,000 micrograms (1 mg.) of riboflavin, whereas the common A-B-D-G pills contain about 50 micrograms (3 micrograms of riboflavin = 1 Sherman-Bourquin unit of vitamin G [B_2]).

Explanation of Figure 3

Fig. 3.—Patient with typical rosacea keratitis accompanied with flushed skin, telangiectasia, thickening of the subcutaneous tissue over the brow, malar prominences and rhinophyma. The patient has had recurring attacks of rosacea keratitis for about three years. Riboflavin has been given for eighteen months. The severe vascularization at the periphery of the cornea cleared almost entirely within four days after she took 3 mg. of natural riboflavin daily, and she has remained free from symptoms, with a white eye, for as long as five months at a time while she took this amount of riboflavin. During this eighteen month period the treatment with riboflavin was interrupted nine times. Each time new rosacea ulcers developed or activity recurred in areas previously affected. A cataract extraction was done during the five month period of administration of riboflavin, and the patient was entirely free from the profuse, thick, yellow discharge that so consistently is present after corneal section. Another obvious feature was the loss of the pink color in the skin, not only of the brow and cheeks but of the exposed neck. At the end of the five month period of riboflavin therapy, there were almost no papular and no pustular eruptions on the face.

Explanation of Figure 4

Fig. 4.—Patient with acne vulgaris and typical rosacea keratitis, the latter condition having been present for years. He has taken 3 mg. of natural riboflavin daily over a period of fifteen months. He has had considerable superficial roentgen irradiation and in recent years has been fairly free from pustules. Recurrences of the rosacea keratitis have always developed within eight days after discontinuance of the riboflavin. After again taking riboflavin, he has been relieved of the photophobia, lacrimation and discomfort within three days, and his eye has become white in four or five days. The blanching of the skin over his face is evident in from four to six days. Analysis of the gastric contents showed absence of free hydrochloric acid after administration of histamine.

Figures 3 and 4

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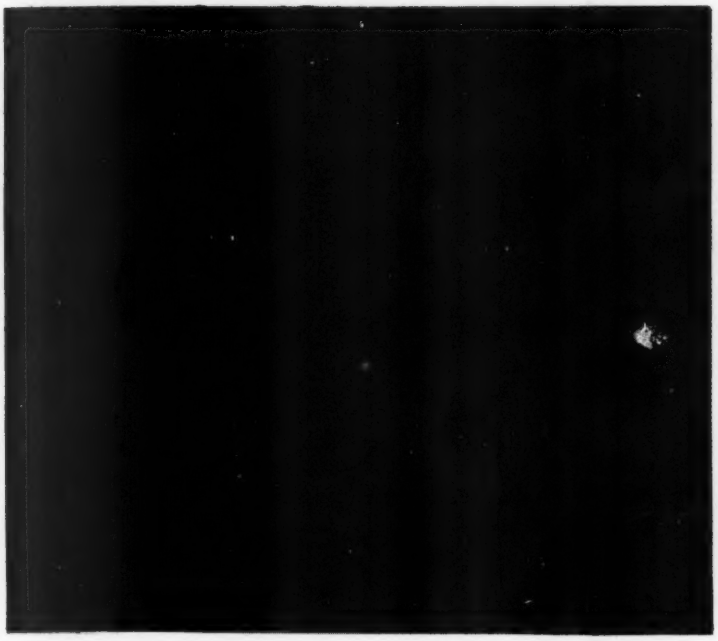
Explanation of Figure 5

Fig. 5.—Patient with rosacea ulcers at the nasal and temporal periphery and conspicuous flushing of the skin and telangiectasia. He drank no milk, ate no liver and ate an egg only occasionally. It was remarkable not only that the keratitis healed within four days after he took 3 mg. of riboflavin daily but that the flushing of his face and the telangiectasia faded so noticeably. There have been no recurrences of the keratitis since he has been eating excessive amounts of eggs, milk and liver.

Explanation of Figure 6

Fig. 6.—Patient showing the association of rosacea keratitis and flushed skin with telangiectasia.



Figures 5 and 6

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fullers' earth in the gastrointestinal tract, or it may have been that patients who had adequate gastric secretion of hydrochloric acid were deprived of even the riboflavin in their diet by adsorption of it to the unsaturated fullers' earth. This form of preparation was discarded as entirely unsatisfactory. 3. An elixir of riboflavin, each teaspoonful containing 1 mg. of natural riboflavin, or an elixir of B complex, each teaspoonful containing 1 mg. of riboflavin as well as therapeutic amounts of the whole B complex. 4. A sterile solution, each 5 cc. containing 1.5 mg. of natural riboflavin, given once to three times daily by intravenous injection. This was the most effective form. The amount of riboflavin supplied by it greatly exceeds the maintenance level, but clinical improvement is phenomenal and is usually maintained by continued oral administration.

In all, 36 patients with rosacea keratitis were treated by the addition of riboflavin to the diet. Of these, 9 also showed some cutaneous type of rosacea. Thirty-two of these patients had prompt healing of the corneal lesions and no recurrences during therapy with riboflavin. Four patients responded slowly or not at all and failed to remain free from symptoms.

Of the 9 who had also cutaneous rosacea, 4 showed satisfactory improvement of the skin of the face. Five appeared to be not improved and had achlorhydria, as demonstrated by the histamine test. The 4 patients who remained free from cutaneous rosacea have been observed for three, four, four and seven months and have not been persuaded to subject themselves to an analysis of their gastric contents.

Such an analysis was done for only 6 of the 32 patients who remained free from ocular rosacea. These 6 had normal levels of gastric hydrochloric acid. Of the 36 patients studied, only 2 gave a history of having eaten adequate amounts of egg white, liver and milk. These 2 patients did not improve with the addition of riboflavin to their diet, and analysis of their gastric contents after the administration of 3 mg. of histamine did not show any free hydrochloric acid.

COMMENT

The 11 patients with so-called rosacea keratitis whose gastric contents were anlyzed for free hydrochloric acid may be subdivided as follows:

1. Patients (6) whose diet was deficient in foods naturally rich in riboflavin but who showed no abnormality in secretion of gastric hydrochloric acid.

2. Patients (2) whose diet appeared to contain an adequate amount of riboflavin but whose gastric contents showed reduced secretion of free hydrochloric acid.

3. Patients (3) whose diet appeared deficient in foods rich in riboflavin and whose gastric contents were achlorhydric.

It would appear, further, that the 36 patients to whom at least 3 mg. daily of natural riboflavin has been administered orally may be subdivided thus:

1. Patients (32) who apparently ate a diet deficient in riboflavin and who remained free from symptoms during oral supplementation of riboflavin (this group included 6 patients with a normal level of gastric hydrochloric acid).

2. Patients (4) who continued to have remission of the keratitis while the diet was supplemented with riboflavin, administered orally, but who also did not secrete any free hydrochloric acid, according to analysis of their gastric contents.

If dietary deficiency of riboflavin results in an inadequate amount of Warburg's yellow enzyme and in faulty tissue oxidation, then there may exist two situations from which rosacea keratitis could arise:

1. Normal diet and faulty secretion of various factors, one of which is free hydrochloric acid.

2. Normal gastric secretions and a diet deficient in riboflavin.

Clinical experience may show that partially deficient gastric secretions may be augmented by an excessive intake of riboflavin.

A series of patients who have achlorhydria are being given riboflavin by intravenous injection, but the difficulty in securing cooperation from all these patients has hindered the completion of the studies. It is evident, however, that riboflavin administered intravenously will arrest the progress of rosacea keratitis in those who have abnormal gastric secretions. The riboflavin, probably, is phosphorylated in the blood.

Also incomplete at this time are our studies concerning demodex organisms removed from the pustules of patients with rosacea. It appears that we are able to inoculate the flushed skin of rats fed diets deficient in riboflavin but not the skin of normal rats. If this is true, Demodex is a secondary invader of a skin which contains telangiectasia and fine, very superficial blood vessels as a result of chronic riboflavin deficiency. It may be that the hyperplasia of the subcutaneous tissue is the result of long-standing irritation by the feeding Demodex.

In this connection it is interesting that György [16] observed: "Chronic riboflavin deficiency in rats is often accompanied by pediculosis. This disease has never been observed in rats manifesting symptoms of a deficiency of other factors of the vitamin B_2 complex. Administration of riboflavin by mouth has a curative effect on this type of pediculosis in

16. György, P.: Pediculosis in Rats Kept on a Riboflavin-Deficient Diet, Proc. Soc. Exper. Biol. & Med. **38**:383, 1938.

rats." This same superficial vascularization of the skin may have favored the feeding habits of these pediculi.

The view that acne rosacea and rosacea keratitis result from deficiency of riboflavin in the diet as a precursor of Warburg's yellow enzyme is supported by the following facts:

1. Administration of a potent preparation of riboflavin in adequate amounts results in clinical improvement and freedom from remission during administration.

2. In man, the tissues involved are those usually exposed to sunlight. In rats, symptoms of riboflavin deficiency are accelerated by exposure of the head and eyes to direct sunlight.

3. Formation of new blood vessels, telangiectasia, corneal vascularization and distention of vessels may possibly be part of the physiologic response of blood vessels to deficient oxidative reactions.

SUMMARY

Thirty-six patients with clinical rosacea keratitis were treated with riboflavin administered orally. Four who did not respond satisfactorily showed altered secretions of the gastric mucosa, at least as far as concerns the free hydrochloric acid. Nine of these 36 patients had also cutaneous rosacea. Others had acne vulgaris, telangiectasia of the skin of the face and seborrheic dermatitis. Emphasis is placed on the similarity between the condition of the eyes of persons with rosacea keratitis and the condition of the eyes of rats in which ulcers developed because of deficiency of riboflavin in the diet. The mechanism is possibly that of inadequate oxidation of enzymes, such as Warburg's yellow enzyme, in the avascular cornea.

Rosacea keratitis (so called) may be the direct result of deficiency of riboflavin, one of the factors in the vitamin B_2 complex. Riboflavin therapy may likewise be of value in certain other forms of corneal vascularization. It apparently is of no value in conditions accompanied by large blood vessels or in other injuries in which scar tissue is present. For constant benefit, continuous therapy is advisable.

POSTURE TREATMENT OF THE IRIS IN LEVER ACTION INTRACAPSULAR EXTRACTION OF CATARACT

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The publication of the papers entitled "Lever Action Operation for Intracapsular Extraction of Cataract" [1] and "Role of Nonviolence in Lever Action Intracapsular Extraction of Cataract" [2] in the ARCHIVES has aroused a world-wide interest in this new method of extraction. I have received many personal communications of inquiry and criticism from learned ophthalmologists from different parts of the globe.

In this paper I shall attempt to answer these communications. The criticism has been leveled principally against my reference to the magic performance of 700 operations in a day by a friend of mine. This statement has been challenged by many readers as an impossible feat and by others as a typographic error. It has been mildly censured by the few who have studied operations for cataract in India and have made the acquaintance of this veteran operator. Thus, one critic retorted that though this statement might be true, he himself would not have written it. Another ophthalmologist who has been to India four times and who recognized the surgeon referred to, wrote: "I believe he did it, although how could he do 700 in a day unless he began very early in the morning and worked most of the night and had four operation tables; but I believe he did it. But I can't make anybody else believe he did." This is the considered opinion of an eminent ophthalmologist who "is in the know."

In my case I owe an explanation to both the believers and the nonbelievers. There is some reason for my making such a controversial statement. At the outset, I must admit that I do not approve of the gigantic performance of my friend, although it cost him much privation and labor. He had to forego his breakfast and dinner also that day. I have strong and conscientious objections to a Derby race in the speed competition of cataract operations. It is, in my opinion, not the number

1. Dutt, K. C.: Lever Action Operation for Intracapsular Extraction of Cataract, Arch. Ophth. **18**:897 (Dec.) 1937.

2. Dutt, K. C.: Role of Non-Violence in Lever Action Intracapsular Extraction of Cataract, Arch. Ophth. **21**:8 (Jan.) 1939.

of operations but the quality that one should try to maintain. The aim should be perfection in the performance of the operation and perfection in the cure. One eye operated on with exquisite perfection and perfect cure without any defect is better than a hundred eyes badly operated on and defectively cured. The human eye is too precious to be operated on haphazardly. Moreover, cataract extraction is too delicate an operation to be performed in haste. A slight deviation in the strategic line of incision or slight excess in the application of power during extraction may mean a great difference in the result. An operation for cataract demands of the surgeon mental equilibrium, delicate sense of touch, keen observation and balanced coordination of all the sense organs, along with exquisite, nonviolent manipulations of magic fingers. A slight indiscretion or absentmindedness on the part of the surgeon means much trouble to the patient, which may end in loss of the eye. I, therefore, could not but frankly tell my friend that the results of his operations were far from satisfactory, to which he replied that one could not expect better results in mass production. I then told him that if he would practice my lever action operation he could at least avoid the loss of vitreous and rupture of the capsule, even when operating at his tremendous speed. However, I must give credit to this surgeon for bestowing the benefits of intracapsular extraction of cataract on thousands of sufferers, and gratuitously too.

The fact that one surgeon gets 700 patients for operation in a single day is proof of my statement: "It is well known that at least 100,000 persons with cataract are operated on in India every year. And still there remain some 500,000 reserves. It will thus be evident that the benefit of extraction of cataract has not yet been universally bestowed. . . ." In order that this may be brought about, it is necessary that an intracapsular method be inaugurated which is easier and simpler than capsulotomy and safer and surer than other intracapsular methods.

In the evolution of cataract operation, capsulotomy and intracapsular methods, both original and modified, are being evolved. It is the general trend of opinion that intracapsular extraction is the ideal method. But as the prevalent methods of intracapsular extraction are mostly complicated in their technic and difficult to perform without loss of vitreous or rupture of the capsule, these cannot be universally acceptable, even though the end result is good visual acuity and the patients are free from iritis and after-cataract. The lever action intracapsular extraction, on the other hand, is free from the defects and difficulties of other intracapsular methods and at the same time is free from all risks. Moreover, it is simpler and easier as well as safer and surer than capsulotomy, as will be presently considered. It insures maximum visual acuity by removal of the lens in its entirety, enclosed within its capsule, thus leav-

ing clear media for all time. The vitreous is undisturbed, and therefore there is neither loss of vitreous at the time of operation nor risk of opacification afterward. No instrument is inserted into the eye except the cataract knife. Thus there is no irritation, trauma or ectopia of any of the internal structures of the eye, and hence the postoperative period is uneventful. The method also takes less time than any other method and insures freedom from irritation and inflammation of the external structures of the eye as well as of the internal structures.

But with all these advantages which render the so-called ideal intracapsular extraction practical for and practicable by surgeons of ordinary skill and also applicable to senile cataracts of all descriptions, simple or complicated, and to all stages of cataract formation as well, one cannot attain the ideal operative results unless one can eliminate insult on that highly sensitive and vascular membrane called the iris. Smith [3] stated: "It is clear that we shall not have perfected the operation for cataract until we can do without an iridectomy as well as extract the lens in its capsule."

Smith, in order to perfect his method, tried in a large number of cases all sorts of devices adopted by other great surgeons and also his own special devices, such as a limbic incision, ending in the cornea 2 mm. in front of the limbus; complete paralysis of the orbicularis muscle by injection of various drugs, such as quinine and urea hydrochloride; elevation of the whole thickness of the eyebrow by means of sutures attached to a piece of adhesive plaster over the forehead; through and through stitches into the scleral and corneal lips of the operative wound, and other methods, but all in vain. At last he came to the conclusion that some sort of iridectomy is necessary to prevent prolapse of the iris and that heavy mydriasis, paralysis of the orbicularis muscle and similar measures are of uncertain value.

In the paper entitled "Role of Nonviolence in Lever Action Intracapsular Extraction of Cataract," it was stated that to insure successful results and an uneventful postoperative period lever action intracapsular extraction among other things observes strict nonviolence to the eye and especially to its internal structures. But regardless of how delicate the operative technic is, there is always the problem of trauma to the tissues. With lever action the irreducible minimum of violence required for extraction of cataract has been worked out. This technic consists of (1) a limbic incision into the upper half of the sclerocorneal arc and (2) delivery of the lens in its capsule by lever action with a minimum of force or effort applied from the outer surface of the eye. The technic,

3. Smith, H.: Treatment of Cataract and Some Other Common Ocular Affections, ed. 2, London, Butterworth & Co., Ltd., 1928, p. 89.

therefore, is "simple extraction of cataract by lever action without iridectomy." Moreover, it is simpler than extraction by simple capsulotomy.

With simple capsulotomy, the capsule is cut either with the capsulotome or by a maneuver of the cataract knife while making the limbic incision. In cutting the capsule with the capsulotome, an additional instrument is inserted into the eye which is not required with the lever action technic. Cutting the capsule with the cataract knife requires extra skill in order to avoid wounding the iris. This is not necessary with lever action. For this reason, lever action is simpler than simple capsulotomy and also is free from the risk of irritation caused by insertion of an extra instrument into the anterior chamber and from the risk of injuring the iris. With simple capsulotomy, complete dilation of the pupil is imperatively necessary for cutting the capsule widely and for expressing the nucleus and cortical matter of the lens. Daily disturbance of dressings in order to instill atropine for the purpose of keeping the pupil dilated is also unavoidable with capsulotomy. On the other hand, with lever action intracapsular extraction, dilatation of the pupil is not required for delivery of the lens-in-capsule. The reason for this is that when the lower edge of the lens-in-capsule rotates by lever action and puts its nose into the pupil, the pupillary passage automatically dilates sufficiently, due to the pressure of the advancing lower edge of the lens-in-capsule, to allow safe delivery. Nor is it necessary to keep the pupil dilated after operation, because there is no risk of tags of cut capsule or of lens matter in the anterior chamber getting entangled with the intact iris there, as is the case with capsulotomy. Hence, the dressings do not need to be disturbed and the operative wound may have perfect rest for three days at a time. Dressings are changed only on the fourth and the seventh day. Noninterference with the dressings aids healing by first intention.

The main purpose of iridectomy, complete or partial or of the peripheral buttonhole type, is to guard against postoperative prolapse of the iris. If iridectomy is not done, how can prolapse be prevented when simple lever action intracapsular extraction is performed? It is well known that there are many causes for postoperative prolapse of the iris. One of the important of these is the involuntary spasm of the orbicularis muscle during the first few hours after extraction. With lever action extraction this is prevented by akinesia of the facial nerve, produced by the injection of a 2 per cent solution of procaine hydrochloride below its crossing at the zygomatic arch, according to the Van Lint[4] technic. This injection paralyzes and prevents the reflex irrita-

4. Van Lint: Paralysie palpébrale temporaire provoquée dans l'opération de la cataracte, Ann. d'ocul. **151**:420, 1914.

tion of the branches of the facial nerve supplying the orbicularis muscle for a few hours after operation. For nervous patients a good dose of a bromide or some other sedative is sometimes given before the operation as an additional measure. This keeps the patient quiet and produces refreshing sleep for a few hours after the operation.

The other important cause of prolapse of the iris is the upward flow of the newly formed aqueous, which carries the upper portion of the iris with it through the operative wound. This can be prevented when using the lever action as technic by posture treatment. After the operation, the patient is gently laid on a bed, the head of which has been raised 9 inches (23 cm.). As water always flows to the lower level, the newly formed aqueous gravitates toward the lower level of the aqueous chamber and accumulates within the uncut lower portion of the cornea and the hyaloid fossa of the vitreous. This accumulation produces a bagging of the lower half of the intact iris, which is effective in dragging down the upper half of the intact iris to a certain extent. Thus, during the outflow of the excess of newly formed aqueous through the operative wound, the iris cannot float upward. The scientific principle of gravitation is taken advantage of in the lever action operation till the danger of prolapse is over. It is common knowledge that the iris may prolapse up to the sixth day after operation. Therefore, after the second dressing on the morning of the seventh day, when the risk of prolapse is over, the head of the bed is brought down to a level with the foot. I have found that raising the head of the bed 9 inches does not inconvenience the patient, but that raising it higher does.

Twenty-four hours after the operation, the patient is made to sit up in bed for some time and for a longer period on subsequent days. This helps to increase the amount of pull on the iris toward the patient's feet. To keep the senile patient continually on his back for more than twenty-four hours is tiresome. To help him to sit up in bed quietly after twenty-four hours gives him much relief and at the same time adds to the mechanism of downward pull on the iris by the accumulation of aqueous in the lower half of the aqueous chamber.

In all cases in which the intraocular tension is lower than normal or is normal, simple lever action operation is performed without iridectomy and the head of the bed is raised 9 inches after the operation. This posture has been found to be effective in preventing prolapse of the iris or drawing up of the pupil. But in the cases in which the intraocular tension is higher than normal, with a tendency to glaucoma, either complete iridectomy or peripheral buttonhole iridectomy must be done in addition to postoperative raising of the head of the bed in order that prolapse of the iris may be successfully guarded against. Buttonhole iridectomy in the iris at about 12 o'clock serves as a sort of safety valve to the outflow of the excess of intraocular lymph. It thus relieves

high tension and guards against prolapse. In order that the buttonhole may function, it is necessary that a solution of physostigmine salicylate (a 1 per cent concentration is used) be dropped into the eye to keep the iris taut by contraction. Moreover, as flabbiness of the iris after the operation allows the upper portion of the iris to be easily ballooned up and floated out of the wound, instillation of this drug into the conjunctiva gives tone to the musculature of the iris and thus guards against its prolapse.

As a rule, no mydriatic is required for the purpose of dilation of the pupil during the delivery of the lens-in-capsule by the simple lever action technic. However, in the case of opium eaters with pinpoint contraction of the pupil, some mydriatic is necessary to counteract the action of opium and to relax the state of rigid contraction of the pupil. Atropine is not required, because prolonged dilatation of the pupil is not necessary. A 2 per cent solution of homatropine hydrobromide instilled several times before operation will overcome the action of opium and dilate the pupil.

Complete iridectomy is done in cases of iritis of long standing with posterior synechiae for the purpose of detaching completely adhesions of the iris to the anterior capsule of the lens before rotation and delivery of the lens-in-capsule are attempted. After the iridectomy is done, a bent spatula is passed behind the iris through the iridectomy opening and turned around. This maneuver is gently and nonviolently done, so as not to pull on the root of the iris. It is well known that a violent pull on the periphery of the cut iris may detach the pillars of the coloboma from its base. When the adhesions of the iris to the anterior capsule are separated, a drop of solution of epinephrine hydrochloride (1:1,000) followed by a drop of a 1 per cent solution of berberine sulfate should be instilled into the eye. Epinephrine stops the hemorrhage. Berberine sulfate acts as a mild astringent, antiseptic and antiphlogistic and therefore helps to soothe the traumatized area antiseptically. The solution of berberine sulfate has been found by me to be beneficial and efficacious and at the same time perfectly harmless and nonirritant. Any surgeon who experiments with it will find that it is most suitable for this purpose. When the hemorrhage stops, the lens in its capsule is rotated on a hyalonavicular fulcrum with a mango leaf dislocator and delivered by lever action. The pillars of the iris are readjusted, and the conjunctival flap is put into situ. The iridectomy is done at 12 o'clock. The gap in the iris is mostly covered by the upper eyelid, and thus photophobia is prevented to a large extent. In all complicated cases in which atropine is indicated during postoperative treatment, complete iridectomy should be preferred to the buttonhole type, because the buttonhole closes under mydriasis with atropine and therefore cannot function as a safety valve.

The merits and faults of simple cataract operation and of combined operation have been much discussed. With capsulotomy, dilation of the pupil is necessary for the purpose of cutting the capsule widely and for expressing the nucleus of the lens. With simple capsulotomy, as pointed out by Hepburn,[5] there is difficulty in expressing the nucleus and cortical matter of the lens and there is risk of prolapse of the iris. Prolapse may take place at the time of expression of the lens or during the postoperative period.

With Barraquer's [6] suction method of upright delivery of the lens-in-capsule with the upper edge foremost and with the forceps-traction method of delivery with the upper edge of the lens foremost and delivery aided by external pressure, complete iridectomy is employed. It is necessary that this procedure be carried out, so that the upper edge of the lens-in-capsule may be grasped high up and have a clear passage when drawn out by traction with the suction cup or with the capsule forceps. In order to avoid capillary attraction, a boat-gliding method is adopted. However, when upright delivery of the lens-in-capsule is being carried out by the boat-gliding movement over the hyaloid fossa of the vitreous, it is necessary that the attachments of the zonule of Zinn be previously detached completely, as are the anchors of a boat set on a muddy dock, before this movement is possible. Moreover, to detach the zonule completely by side to side and to and fro movements of the lens-in-capsule, held by the vacuum suction cup or the capsule forceps, complete iridectomy is required so that sufficient space for free movement is available.

Hess [7] advocated peripheral iridectomy. This has the special advantage of keeping the sphincter iridis uncut and capable of reacting to light and thus preventing the dazzling produced after complete iridectomy. The peripheral buttonhole acts as a sort of safety valve for the outlet of the excess aqueous.

Smith [8] advocated a rather broad iridectomy, or three peripheral buttonholes instead: two at the bases of the incision at 3 o'clock and 9 o'clock and a third at 12 o'clock. He found that although a single buttonhole at 12 o'clock often prevented prolapse of the iris at that

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5. Hepburn, M. L.: The Extraction of Cataract, Brit. J. Ophth. **2**:300, 1918.

6. Barraquer, I.: (*a*) Intracapsular Method of Cataract Extraction, Brit. M. J. **2**:666, 1924; (*b*) Extracción ideal de la catarata, Arch. de oftal. hispano-am. **17**:252, 1917; (*c*) Dangers of Capsulotomy and Advantages of Complete Extraction, Arch. Ophth. **50**:307, 1921; (*d*) Phakoerisis, ibid. **51**:448, 1922; (*e*) Facoerisis, in Fisher, W. A.: Cataract Senile, Traumatic and Congenital, Chicago, H. G. Adair Printing Co., 1917, p. 28.

7. Hess, C.: Bemerkung zu dem Aufsatze von Elschnig über Staroperation, Arch. f. Augenh. **70**:80, 1912.

8. Smith, H.: (*a*) Extraction of Cataract in Its Capsule, Arch. Ophth. **33**: 64, 1904; (*b*) New Technique for Expression of Cataractous Lens in Its Capsule, ibid. **55**:213, 1926; (*c*) in discussion on Knapp,[10b] p. 123; (*d*) footnote 3, p. 97.

location, prolapse sometimes took place through the bases of the operative wound. To prevent prolapse completely, therefore, three buttonholes are required. Smith used an ointment containing physostigmine salicylate in the after-treatment to stretch open the buttonholes and to keep the iris sheet taut, so as to lessen its liability to adhere to the wound.

With lever action intracapsular extraction, three small conjunctival flaps are advisedly fashioned at the strategic points where Smith makes three buttonholes, i. e., two at the two bases of the incision, at 3 o'clock and at 9 o'clock, and a third, or terminal, conjunctival flap at 12 o'clock. At these three vulnerable points the three small conjunctival flaps with thin layers of subconjunctival tissue underneath them quickly agglutinate with the raw episcleral wound and cement the points of prolapse. The conjunctival flaps also serve to keep the margins of the operative wound in apposition and prevent gaping. Prolapse of the iris at these points is thereby guarded against by the rapid union of the three conjunctival flaps and sealing up of the three vulnerable points. Toned up and tense by the action of physostigmine salicylate, the iris cannot be ballooned up. Dragged down by the bag of aqueous accumulated within the lower half of the aqueous chamber owing to raising of the head of the bed, the iris can no more be easily floated out. Then again, when the three vulnerable points for prolapse of the iris are sealed by conjunctival flaps, the chances of prolapse are minimized. All the three devices, therefore, combine and help each other in successfully preventing prolapse of the iris when lever action intracapsular extraction of cataract is done.

Verhoeff [9] advocated vertical complete slitting of the iris from 12 o'clock to the upper margin of the pupil. He first cuts off a small bit of iris at about its base and then passes one blade of the iris scissors through the cut behind the iris. The other blade is passed in front of the iris till the points of the scissors reach the pupil. The blades are now closed, and the iris is thus slit open vertically from the base at 12 o'clock to the margin.

For his usual method of tumbling, Barraquer [6] makes a peripheral buttonhole in the iris, and for the Knapp [10]-Török [11]-Elschnig [12] method

9. Verhoeff, F. H.: Cataract Extraction with Modified Iridectomy, Ophth. Rec. **15**:335, 1906.

10. Knapp, A.: (*a*) Report of One Hundred Successive Extractions of Cataract in the Capsule After Subluxation with the Capsule Forceps, Arch. Ophth. **44**:1, 1915; (*b*) Late Results of Intracapsular Cataract Extraction, Tr. Ophth. Soc. U. Kingdom **45**:117, 1925.

11. Török, E.: Extraction of Cataracts, Ann. Ophth. **25**:712, 1916.

12. Elschnig, A.: Die Intracapsulare Starextraktion, ed. 28, Berlin, Julius Springer, 1932, p. 3; Altersstarextraktion in der Kapsel, Ztschr. f. Augenh. **75**:1, 1931; Extraction of Senile Cataract in Capsule, Am. J. Ophth. **8**:355, 1925.

of tumbling with the lower edge foremost, a slit is made near the root of the iris. But with neither method is complete iridectomy done. The buttonhole or the slit in the iris at 12 o'clock serves to act as a sort of safety valve for the outlet of the excess of newly formed aqueous during the postoperative period.

After having put to test all the devices suggested or employed by learned ophthalmologists for the prevention of prolapse of the intact iris, I have come to the same conclusion as Smith, namely, that they are unreliable. At last, a combination of three simple procedures, (1) posture treatment by raising the head of the bed by 9 inches, (2) toning up of the iris muscles by the use of physostigmine salicylate, and (3) the use of three small conjunctival flaps to guard the three strategic vulnerable points, has been found effective in preventing prolapse of the intact iris in all cases in which iridectomy is not especially indicated for other reasons.

The question may be asked: In consideration of the fact that iridectomy is now being practiced at almost all cataract operations, either capsulotomy or intracapsular extraction, without many bad results, what is the necessity of laboriously hunting some device for avoiding this more or less harmless operation? What advantages may be derived from a simple method of extraction that is devoid of risk of prolapse of the iris? Taylor,[13] in a letter to the editor of the *British Journal of Ophthalmology,* claimed that the advantages of simple extraction are: (1) lack of pain during operation, (2) less bleeding, (3) fewer instruments inserted into the eye, (4) less risk of tags of capsule floating into the operative wound, (5) less risk of prolapse of the vitreous and (6) less likelihood of postoperative increase of tension. It may be added that if the iris is intact and not prolapsed, there will be the advantages of (7) a round pupil without disfigurement, (8) absence of photophobia due to entrance of excess of light, (9) better visual results, (10) normal action of the diaphragm, which contracts and dilates with the amount of light falling on the retina, (11) shorter operative time and (12) less traumatism. Although peripheral buttonhole iridectomy is less objectionable than complete iridectomy and is suitable for lever action intracapsular extraction, it is better to avoid cutting the iris unless it is especially indicated. Iridectomy causes more or less bleeding. A bloodless cataract extraction goes a long way toward obtaining perfection in the end results, which is the aim of lever action intracapsular extraction.

In all cases in which there is a hemophilic tendency, whether acquired or familial or due to low blood calcium or atheromatous arteries with high blood pressure, the surgeon should risk slight prolapse of the iris as being a lesser evil than postoperative hemorrhage, which means

13. Taylor, S. J.: Atropin in Cataract Extraction, Brit. J. Ophth. **2**:117, 1918.

complete loss of eyesight. Three thousand years ago Suśruta [14] cautioned thus: "The surgeon should not operate on a patient who is unfit for venesection because of a hemorrhagic tendency or diseased blood vessels. Let this time-honored warning be heeded, and no iridectomy, not even buttonhole iridectomy, be attempted." In such cases, posture treatment with its two auxiliaries is the sheet anchor.

It may perhaps be argued by some that the three procedures constituting the posture treatment are too simple to attract the imagination. But the grand and the grotesque, however much they may be tempting and attractive, are not productive of best results in cataract operations. Verily, the poet says, "All that glitters is not gold." Scientific technic, simplicity and nonviolence are the basic principles of the lever action intracapsular operation. The trio has been found to be productive of successful results—both the immediate and the end results —and there is nothing like success.

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14. Suśruta Sanhita (dated 1000 B. C.), Uttara Tantra, chap. 17, verse 68. Dutt, K. C.: Cataract Operations in the Prehistoric Age [translation of Suśruta Sanhita], Arch. Ophth. **20**:6 (July) 1938.

EXPERIMENTAL PRODUCTION OF SO-CALLED BULLOUS KERATITIS

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In the course of some experiments on the distensibility of the sclera, an incidental observation was made which led to the experimental production of vesicles and bullae under the corneal epithelium. So far as could be inferred from gross and slit lamp examinations, this experimentally produced condition was the counterpart of what is known to clinicians as bullous keratitis. Since this condition has not heretofore been produced experimentally, so far as I can determine, except by the use of excessive pressure, and as these observations shed new light on the pathogenesis of bullous keratitis, a preliminary report is being made at this time. A detailed report of experiments dealing with the clinical applications, now in progress, will follow at a subsequent date.

In order properly to evaluate the experimental results in the light of the clinical condition, it is necessary first to consider what is meant by bullous keratitis and to mention the current theories of its pathogenesis.

Bullous, or vesicular, keratitis is obviously not a disease entity by itself but a condition found in association with several different pathologic disturbances. That it should be called corneal vesiculation or some such name rather than bullous keratitis is a point well taken, as it is neither inflammatory nor an independent entity.

According to my experience, corneal vesiculation is met with most frequently in association with the following conditions: long-standing glaucoma, Fuchs's epithelial (Vogt's endothelial) dystrophy and postoperative aphakia in which there has been loss of vitreous or in which the vitreous remains permanently in contact with the back of the cornea. I have also observed it, but much less commonly, with various forms of deep-seated keratitis, such as keratitis disciformis, and rarely with interstitial keratitis. It is not immediately apparent what these various diseases have in common that they should all be associated with vesiculation, but it is noteworthy that, with the possible exception of glaucoma, they all are accompanied by a disturbance of the corneal endothelium. Moreover, the superficial vesiculation is local-

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ized to that portion of the cornea corresponding to the disturbance in the posterior portion, so that there can be little doubt of some connection between the epithelial and the endothelial changes. Just where glaucoma fits into this picture is less obvious, but it is altogether possible that the profound alteration in the corneal endothelium which occurs in cases of long-standing glaucoma may be the alteration analogous to the absence of endothelium in the other diseases. In any case it is clear that vesiculation of the surface of the cornea usually, if not invariably, goes hand in hand with disturbances of the posterior corneal surface, and it seems likely that the vesicles, appearing as they do long after the endothelial changes, are dependent on the posterior disturbances.

There is a remarkable paucity of speculation in the literature as to the pathogenesis of corneal vesiculation. The fact that vesicles are supposed to occur in the early stages of herpes simplex of the eye, together with the fact that in most cases of bullous keratitis hypesthesia is present, led some to suggest that all types of corneal vesiculation were neurogenic (Birnbacher and Czermak [1] and Elschnig [2]). Ewing [3] expressed the belief that the bullae were a part of the fatty degeneration in Bowman's membrane. Parsons [4] suggested that vesiculation is due to a disturbance of lymph circulation in the cornea but did not state how this disturbance is brought about.

The most plausible previous theory, and the one most widely accepted, assumes that under certain pathologic conditions fluid from the aqueous percolates through the cornea, finds the epithelium relatively impermeable and lodges in the subepithelial spaces to form the characteristic vesicles (Fuchs [5]).

In support of this theory, Leber's experiments are frequently cited. Leber [6] found that under pressures of 200 mm. of mercury aqueous might be forced through the cornea and that bullae would appear under

1. Birnbacher, A., and Czermak, W.: Beiträge zur pathologischen Anatomie des Glaukoms, Arch. f. Ophth. (pt. 1) **31**:297, 1885; Beiträge zur pathologischen Anatomie und Pathogenese des Glaukoms, ibid. (pt. 2) **32**:1, 1886.

2. Elschnig, A., in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1928, vol. 11, pt. 1, p. 881.

3. Ewing, A. E.: Bullous Keratitis: Fatty Degeneration of Bowman's Membrane, Am. J. Ophth. **21**:161, 1904.

4. Parsons, J. H.: The Pathology of the Eye, London, Hodder & Stoughton, Ltd., 1904, vol. 1, p. 179.

5. Fuchs, E.: Ueber die Trübung der Hornhaut bei Glaukom, Arch. f. Ophth. **27**:66, 1881.

6. Leber, T.: Circulations- und Ernährungs-Verhältnisse des Auges, in von Graefe, A., and Saemisch, E. T.: Handbuch der gesamten Augenheilkunde, ed. 2, Leipzig, Wilhelm Engelmann, 1903, vol. 2, pt. 2, chap. 11, p. 275.

the epithelium. Parsons [7] pointed out, however, that the excessive pressure found necessary by Leber excluded this as the mechanism, as even the highest tension found in cases of glaucoma would be below the pressure found necessary by Leber. When Leber [8] removed the endothelium hydrops of the cornea developed in which bullae were an occasional feature, even in the presence of normal tension; but the massive swelling of the cornea apparently bore no resemblance to bullous keratitis, nor is it evident that the fluid was in fact aqueous.

Before undertaking the series of experiments by which corneal vesiculation was produced, I had unsuccessfully attempted to produce bullae by forcing fluid through the corneas of enucleated dogs' eyes. I found that when a cannula was introduced through the optic nerve and a pressure equivalent to 70 to 100 mm. of mercury maintained for more than a few minutes, tiny beads of fluid appeared on the surface of the cornea. These droplets, which gave the cornea an appearance of sweating, apparently came through from the anterior chamber, but no vesicles or bullae were found at any time. Fluid was also forced through the cornea without any elevation of the intraocular pressure by immersing the whole eye or just the corneal portion of the whole eye in hypertonic saline solution (10 and 20 per cent) for about one hour. At the end of this time the eye had obviously lost fluid, as it was much more collapsed than formerly, and a good part of the fluid had come from the anterior chamber, which was now quite shallow. But again no vesicles or bullae were present.

Having failed to produce corneal vesiculation by a method analogous to that which is believed to take place clinically, I undertook the following experiments, which show not only how it may be produced experimentally but how it may be "cured" once it has developed.

EXPERIMENTS

Immersion of the Whole Eye.—The following experiments were performed with approximately 15 enucleated dogs' eyes and several cats' eyes. Most of the eyes were enucleated two to three hours post mortem, but several were not studied for one or two days, having in the meantime been kept in the ice box in physiologic solution of sodium chloride.

First, the eye under observation was placed in one of several hypertonic solutions for three to four hours. The solutions used were sodium chloride (2.5, 10 and 20 per cent) and sucrose (5 per cent). After thorough saturation with hypertonic solution, the eye was then removed and placed in a vessel containing either distilled water, tap water or physiologic solution of sodium chloride.

Results.—After being removed from the hypertonic solution and put in the relatively hypotonic solution again, the eye showed corneal

7. Parsons,[4] 1908, vol. 3, p. 986.
8. Leber,[6] p. 359.

edema and superficial haze within a few minutes, and after a somewhat longer time, varying between five and ten minutes, depending on the concentration of the hypertonic fluid in which the eye had previously been exposed, distinct vesicles appeared. These were at first evident in reflected light only but increased in size during the subsequent fifteen to thirty minutes to become distinct bullae. If the eye was left in the relatively hypotonic fluid long enough, and if it had previously been thoroughly saturated with 10 to 20 per cent saline solution, the bullae progressively increased in size, became confluent and ultimately elevated most, if not all, of the epithelium.

When the eye was removed from the hypertonic solution, the intraocular pressure was very low, but after it was put in hypotonic solution the pressure rose. But that this rise in pressure was not responsible for the vesiculation was shown by opening the sclera and then immersing part of the eye, cornea downward, in hypotonic solution, whereupon vesiculation occurred as formerly, although the intraocular pressure was negligible.

The vesiculation was equally apparent in eyes studied one to two days post mortem and in fresher eyes.

There was no marked difference in the results with the various concentrations of salt solution, but in general the greater the hypertonicity of the fluid the more rapid and intense was the development of vesiculation when the eye was placed again in hypotonic solution. With the weaker concentrations (2.5 per cent), vesicles occurred, but they did not always progress to the stage of large bullae, as was the case with the stronger concentrations. Five per cent sucrose solution had approximately the same effect as 10 per cent salt solution.

Several variations of the foregoing experiments were made. The corneas of two fresh eyes were excised and put first into 10 per cent saline solution and then into water. In one, corneal edema occurred but no definite vesiculation; in the other, typical vesicles and small bullae (1 to 2 mm.) appeared near the limbus. Another variation of the foregoing experiments was performed as follows: After being in 10 per cent saline solution for several hours, an eye was removed and placed in liquid petrolatum. Here again, corneal edema occurred with a superficial opacity. But the corneal edema developed less rapidly than when the eye was placed in water and did not progress to the stage of vesicles and bullae.

Injection into the Anterior Chamber.—About 15 enucleated dogs' eyes and several cats' eyes were used. Most of the dogs' eyes were studied two to three hours post mortem. Observations on the cats' eyes were made on eyes both immediately after enucleation and in vivo. Cats seemed to offer a particularly favorable opportunity for these observations on the living animal because of the large size of their anterior chambers.

Enucleated Eyes: Saline solution in concentrations of 20, 10 and 2.5 per cent and sucrose solution in a concentration of 5 per cent were injected into the anterior chamber after removal of as much aqueous as possible. The actual concentration in the anterior chamber in each case is, of course, unknown, but obviously it is less than the foregoing percentages. The injections were made into the anterior chamber through the limbus and, via the optic nerve, through the vitreous and lens. The latter method was found by far the best in enucleated eyes, as there was minimal leakage and no danger of contaminating the surface of the cornea with the hypertonic fluid. After the injection, the eye was placed in water.

Eyes in Vivo: Two cats under pentobarbital anesthesia were used. A needle was inserted into the anterior chamber at the limbus, the aqueous evacuated and saline solution injected. The concentration of saline solution used in two eyes was 20 per cent and in the other two eyes, 10 per cent. In 1 instance, after the injection an iontophoresis glass containing water was placed on the eye, and in another instance a few drops of 10 per cent saline solution was dropped on the cornea. In both cases the cornea was partially protected by the nictitating membrane.

Results.—After the injection of hypertonic solution into the anterior chamber, vesiculation and bullous formation occurred the same as after immersion of the whole eye in hypertonic and then in hypotonic solution. But whereas it was necessary with immersion to keep the eye in hypertonic solution two to three hours, by injection of hypertonic solution the vesiculation could be produced much more acutely. It was only necessary that the surface of the cornea be kept moistened with a relatively hypotonic fluid. This fluid may be water, physiologic solution of sodium chloride or tears. However, in the living eye when the cornea was partially protected by the nictitating membrane and the rest of the cornea exposed to water, vesiculation occurred more intensely in the exposed portions than under the nictitating membrane. On the other hand, when hypertonic saline solution was dropped on the cornea, vesiculation was most intense under the nictitating membrane. In other words, decreasing and increasing the tonicity of the fluid outside the eye produce an opposite effect on the process of vesiculation.

In none of the eyes in which salt solution was injected did an abnormal tension develop during the course of the observations.

The following variation of the foregoing experiments was carried out on the enucleated eyes: The surface of the cornea was dried first with fine filter paper, and then the eye was placed near a fan to promote further drying. When 10 per cent saline solution was now injected into the anterior chamber, no vesiculation of the cornea occurred. Thus some moisture on the outside of the cornea is essential for the process.

Also, a comparison was made between the enucleated eyes in which the endothelium was presumably intact and those in which it was scratched by the point of the needle before the saline solution was injected. No difference was observed.

Most interesting of all is the reversibility of the vesiculation. If an eye into which hypertonic saline solution has been injected is placed in water

until a well developed corneal vesiculation with bullae has developed and then is placed back in the hypertonic solution, the cornea will again become clear within a few minutes and the bullae will disappear. The possibility of applying this "cure" clinically will be discussed in a subsequent paper.

COMMENT

The basic question is, of course, whence comes the fluid responsible for the corneal edema and vesiculation? There is on the one hand the currently held theory that it is derived from the aqueous, and on the other hand the theory, suggested by these experiments, that it is derived from the fluid outside of the eye. The theory that it comes from the aqueous, and for which the experiments of Leber are frequently cited, was essentially denied by Leber.[8] He pointed out that when the endothelium was intact the cornea was effectively impermeable to aqueous and that the removal of the endothelium caused a deep corneal condition somewhat suggestive of interstitial keratitis. He made no mention of any likeness to bullous keratitis.

An equally simple explanation, and one which is more consistent with the foregoing facts, would base the corneal vesiculation on osmotic attraction of fluid from the outside into the cornea. The one prerequisite for the development of experimental vesiculation is a relative hypertonicity of the fluid within the eye compared with that on the outside. Given this condition experimentally vesiculation invariably occurs. The question must remain open as to whether or not this condition pertains to clinical cases of bullous keratitis, but there is some evidence that it does. Normally the tears are ever so slightly more hypertonic than the corneal and aqueous fluid (Ridley[9]). The additional osmotic force of the tears, due to the higher protein content, may be sufficient to prevent vesiculation normally, but it is nevertheless so small that an increase in the osmotic force of the cornea would not have to be great to reverse the normal balance. It is, therefore, extremely interesting that in the one condition in which bullous keratitis occurs most commonly, namely, glaucoma, Fischer[10] has reported a characteristic increase in the salt content of the cornea. So far as I am aware, no measurements of the corneal osmotic tension have been made in other clinical conditions associated with bullous keratitis.

These observations bring up several questions which I shall attempt to answer. First, what is the significance of the endothelial defect in most clinical cases of corneal vesiculation, and second, why do the bullae form in the subepithelial regions with no marked changes in the stroma?

9. Ridley, F.: The Intraocular Pressure and Drainage of the Aqueous Humor, Brit. J. Exper. Path. **11**:217, 1930.

10. Fischer, F. P.: Der Wasserhaushalt des Auges und seiner Teile. Docum. ophth. **1**:79, 1938.

If it is correct to assume on the one hand that the same mechanism underlies the experimental and clinical vesiculation and on the other hand that an endothelial defect is the forerunner of the clinical condition, one must assume that the presence of an endothelial defect alters the chemical constitution of the cornea in such a way as to increase its osmotic pressure (increase in salt content?). Leber has indeed shown that in the presence of an endothelial defect there is a greater tendency for the cornea to take up fluid, and von Hippel [11] has shown that under these conditions fluorescein diffuses more readily into the cornea from the outside. It must be assumed further that this altered chemical balance does not occur or at least is not sufficient to produce vesiculation until the endothelial defect has been present for some time, as the endothelium may be clinically defective for months or years before the epithelial changes occur.

As for the question why the vesicles form in the subepithelial region and not in the stroma, I can again suggest only a tentative explanation. It may, of course, be a simple mechanical effect whereby the dense stroma does not allow the accumulation of fluid in its interspaces as readily as in the subepithelial region. But this is contrary to what is seen occasionally in cases of hydrops of the cornea, wherein the stroma interspaces are distended by fluid without the presence of subepithelial vesiculation. Another, and possibly more acceptable, explanation would be the assumption of a relatively irreversible permeability of the epithelium, whereby water, attracted by the higher salt content of the cornea, diffuses readily through from the outside but not in the reverse direction. This would account for the accumulation of fluid on the corneal side of the epithelium but not specifically in the subepithelial space. To explain this, one must make the further assumption that Bowman's membrane forms a relatively greater barrier to the passage of water than does the rest of the corneal stroma. Given these conditions and a relative hypertonicity of the cornea, fluid will necessarily accumulate in the subepithelial space. Vesicles will not form in the stroma, as the fluid will diffuse into the anterior chamber as rapidly as it passes through Bowman's membrane.

I cannot substantiate nor do I know how to test the second assumption, that Bowman's membrane offers a greater barrier to the passage of fluid than does the stroma, but I know of no facts to the contrary. I should like to point out, however, that the first assumption, regarding the irreversibility of the epithelium, is in entire accord with the observa-

11. von Hippel, E.: Die Ergebnisse meiner Fluoresceinmethode zum Nachweis von Erkrankungen des Hornhautendothels, Arch. f. Ophth. **54**:509, 1902.

tions of Fischer,[12] who found that water would readily enter the cornea, whether the epithelium were present or not, but would leave the cornea only when the epithelium was removed. His findings are apparently explicable only by the assumption of a relative irreversibly permeable epithelium.

CONCLUSIONS

1. It is possible to produce experimentally a condition of corneal vesiculation which is similar to the clinical condition known as bullous keratitis. What evidence is available would make it seem likely that the experimental and clinical conditions have essentially the same pathogenesis.

2. Corneal vesiculation similar to that which occurs in cases of bullous keratitis is not produced by forcing fluid into the cornea from the aqueous unless excessively high pressures are used. The common assumption that clinical vesiculation is caused in this way could not be confirmed experimentally.

3. On the contrary, the mechanism for experimental vesiculation is apparently the absorption of fluid from the outside inward. This occurs when the osmotic tension of the cornea is greater than that of the fluid on the outside of the eye. This relative hypertonicity of the cornea may be artificially brought about by saturating the whole eye with some hypertonic solution or by injecting the solution into the anterior chamber. Vesiculation will then occur when the cornea is exposed to a relatively hypotonic solution, such as water, physiologic solution of sodium chloride or tears.

4. There is some evidence that this mechanism is operative in clinical vesiculation of the cornea and, so far as I know, there is no evidence to the contrary. But the role of the endothelium in bringing this about is open to question. To explain the subepithelial position of the vesicles, it is necessary to assume a differential permeability of the epithelium and Bowman's membrane.

5. Experimental vesiculation of the cornea is reversible. The vesicles and bullae which have been made to appear by immersing the eye in hypotonic solution may be made to disappear by placing it in hypertonic solutions.

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12. Fischer, F. P.: Ueber die Permeabilität der Hornhaut und über Vitalfärbungen des vorderen Bulbusabschnittes mit Bemerkungen über die Vitalfärbung des Plexus choroideus, Arch. f. Augenh. **100**:430, 1929.

VACUUM MASSAGE OF THE EYEBALL

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From early times ocular massage has been recognized as producing a favorable effect on diseases of the eye. Grecian records show such a procedure to have been practiced among that people, and Paul of Aegina, the last of the eclectics, commented on its curative value. Massage of the eyes seems not to have originated with the intellectuals, for the savages of Africa and America used it intuitively.

Pagenstecher [1] in 1871 published a monograph on massage of the eyes, at which time he reported having obtained "magnificent results" by massage even when other agents failed. Donders [1] in 1872 recited his accomplishments with ocular massage before the International Congress of Ophthalmology at London. Heiberg [1] in 1874, Just,[2] Pedraglia [3] in 1880 and Damalix [4] in 1881 particularized special disease benefited by massage.

Hoffmann [5] is credited by Domec [6] with being the first to design an instrument for mechanically massaging the eye.

In the "Encyclopédie française d'ophtalmologie" [7] it is stated:

> Pneumatic massage conceived by Hoffmann, of Ulm, was practiced with the aid of an eyecup well fitted to the globe. To the bottom of the cup a syringe was attached. By up and down movement of the piston the pressure on the globe is increased or diminished.

In the "American Encyclopedia of Ophthalmology" [8] it is recorded that the Victor machine was utilized to massage the eye. (The principle of the machine is the same as that of Hoffmann's instrument but the

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1. Cited by Lagrange, F., and Valude, E.: Encyclopédie française d'ophtalmologie, Paris, O. Doin, 1909, vol. 8, p. 1012.
2. Just, O.: Centralbl. f. prakt. Augenh. **4**:8-11, 1880.
3. Pedraglia, R.: Centralbl. f. prakt. Augenh. **5**:111, 1881.
4. Damalix, A.: Arch. d'opht. **1**:491-499, 1881.
5. Hoffmann, J.: Repert. d. Thierh. **45**:269-272, 1884.
6. Domec, S.: Anjou méd. **6**:185 and 220, 1899; cited by Lagrange and Valude.[7]
7. Lagrange, F., and Valude, E.: Encyclopédie française d'ophtalmologie, Paris, O. Doin, 1909, vol. 8, p. 1013.
8. Wood, C. A.: American Encyclopedia and Dictionary of Ophthalmology, Chicago, Cleveland Press, 1914, vol. 7, p. 4892.

apparatus is more complicated.) The Piesberger instrument is also mentioned, the ocular massage being produced by vibration of a rod held against the eye.

Though ocular massage throughout the centuries has proved beneficial in the treatment of diseases of the eyes, it is now practically abandoned, especially with instruments. The description of a simple device for massaging the eye follows: It has three parts, a cup, a small syringe and a light, as depicted in the accompanying illustration. The cup is carved into one end of a transparent cellulose rod, 12.5 mm. in diameter and 4 cm. in depth. The other end of the rod is threaded and screwed into an Eveready two cell flashlight. The cellulose material transmits the light to the center of the cup. Exteriorly the cup is a section of a 12 mm. sphere. Its inner side is ground to produce a high

The Dimitry luminous ocular massage instrument. It consists of three parts: a flashlight of the Eveready type; a 2 cc. syringe, the upward movement of the plunger being propelled by a spring, and a third part made of a plastic material. At one end of this portion is carved a cup, which is capped, as it were, by a planoconvex lens. The lens is shaped during the carving of the cup and magnifies the tissue. The Eveready flashlight illuminates the cup and the tissue.

power lens for magnifying the tissue massaged. A 2 cc. glass syringe is attached to the cup by means of a cannula; the plunger unit is moved upward in the barrel by a spiral spring.

When putting the appliance into use, the eye is first anesthetized, and then the cup is placed in contact with the eyeball, encircling the cornea. The light is turned on, and the ocular tissue is viewed under the magnification provided in the cup. The cannula of the syringe is attached while its plunger is held down. When the thumb is removed and the pressure released, the spring recoils, the plunger ascends and a vacuum is produced in the cup. This atmospheric change produced

causes the cup to grip the eye, the grip being controlled by the pressure or release of the plunger by the thumb. The intermittent action accomplished by alternate pressure and release of the plunger effects massage of the globe.

Physiologists have long granted that the pneumatic manipulation of an organ produces an increased flow of blood and lymph into its tissue and that such a change increases nutrition and resistance to disease. The clinical reports which follow make it unnecessary to dilate on hypotheses as to how benefit is brought about; the evidence of change in the tissue is obvious. Immediately on massaging the eyeball the cornea is observed to become limpid. Such brilliancy and clearness can be accounted for only by an increase of lymph passing into the corneal tissue. This change in the appearance of the cornea occurs even in the presence of keratitis. After massage, a pinkish flush about the cornea is momentarily observed, evidently a ciliary injection, for there is little or no conjunctival injection. Intraocular tension is reduced and signifies that the vessels on both the outer and the inner side of the globe are affected. That the inner vessels are affected was seen in the altered position of an embolus of a retinal vessel. Changes seem to be produced in the iris tissue, for the iris becomes brighter, with greater definition of its architecture. However, this may be only an appearance in consequence of the increased transparency of the cornea. Massage does not cause the pupil to contract or dilate, yet iris synechiae are broken.

The grip of the vacuum cup is great and may momentarily distort the cornea and even separate its lamellae. If this occurs, it is easily seen that should the cup be allowed to grasp the conjunctiva for any length of time, hyperemia, hemorrhage and even chemosis of this tissue might be occasioned, and it is assumed that necrosis could be brought about.

Attempts to observe the fundus through the cup when in it is contact with the eye have not proved satisfactory. After massage of the eye, it cannot be said that retinal vessels have been altered; however, an embolus, as stated, had been seen to change position. It was observed that ocular massage in cases of simple glaucoma immediately brought about a reduction of the increased tension and that the reduction remained for hours. The incongruous situation was that in cases of certain uveal lesions in which the tension was less than normal, the tension could be brought up to normal or raised above it. When massage was used in cases of punctate or diffused keratitis, clearing was hastened. When it was employed in cases of ulcers of the cornea, the floor of the ulcer showed a definite change. In cases of descemetitis the characteristic triangular deposits became altered in form. Painful conditions were often relieved to a remarkable degree.

Ten patients suffering from glaucoma simplex received ocular massage. The elevated tension of each patient was effected by manipulation of the eyeball and continued to fall for several hours; however, it returned to its original height in the next twenty-four to thirty-six hours. When the massage was repeated the effect lasted much longer, but permanence of effect was doubtful unless the treatment was used in connection with other agents.

Two patients in whom glaucoma developed after extraction of cataract were immediately benefited by massage of the eyeball, and the effect was permanent. Five patients with keratitis were treated by massage. Two of these suffered from the results of an old interstitial keratitis in which the cornea was slow in clearing; the other 3 had an active condition. The entire series of patients was benefited, the cornea clearing. Two patients suffered with uveitis. The tension of both was below normal. Massage raised the tension, yet the patients were relieved of pain and vision was improved. However, dental infection had also been corrected. Massage was repeatedly used in cases of atrophy of the optic nerve to ascertain what effect could be produced on the retinal vessel. At one time it was believed to have dilated them. All members of the examining group could not concur that such was the case.

Two patients with retinitis pigmentosa were treated; the vision of 1 patient increased and the visual field enlarged in a spectacular manner. However, improvement in this case was discounted on the ground that errors may have occurred in taking the visual field and even in recording the vision. The other patient showed no effect from the massage.

Three patients had ulcers of the cornea. All showed improvement after massage, but it must be remembered none of them had a large ulcer. In 2 cases of hypopyon with ulcer of the cornea, the ulcer improved and the hypopyon rapidly disappeared. There was 1 case of embolus of the temporal vessels in which the embolus traveled to the periphery and disappeared.

CONCLUSION

Ocular massage is unquestionably of merit in the treatment of pathologic conditions of the eye, and its employment is simplified by the use of the simple instrument described.

The instrument was made by V. Mueller & Co., of Chicago.

ACUTE EXUDATIVE CHOROIDITIS

PATHOLOGIC PHYSIOLOGY; TREATMENT WITH VASODILATORS

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Acute exudative choroiditis, a not uncommon lesion of the fundus, has been considered to be a disease sui generis. The pathologic appearance of the healed lesion is well known, but reports of the pathologic appearance of the acute lesion are relatively uncommon.

There are no fundamental differences between the lesions of acute choroiditis and of chorioretinitis juxtapapillaris (Jensen's disease) other than that of location in the fundus. In the typical case of acute exudative choroiditis the lesion is surrounded on all sides by normal retina and choroid; in the juxtapapillary type the lesion is adjacent to the disk, so that the edema surrounding the lesion involves part of the nerve head, giving the picture of partial optic neuritis. When the lesion in some of the cases of the juxtapapillary type has become quiescent, it is often seen that the choroidal lesion is not always directly adjacent to the disk but is sometimes separated from it by a small but definite amount of normal-appearing fundus.

The retina overlying the acute choroidal lesion is usually edematous, so that the overlying nerve fiber layer is more or less involved. The question as to whether such a lesion should be called choroiditis, chorioretinitis or retinochoroiditis is of academic interest only; the primary disturbance is in the choroid. Likewise, the presence of opacities of the vitreous indicates a lesion of more marked severity, in which, in addition to the secondary involvement of the retina, plasma and cells have passed into the vitreous. The differences between a simple choroidal lesion, a choroidal lesion with marked edema of the overlying retina and finally one in which there is also a disturbance of vitreous are quantitative rather than qualitative.

An arcuate or cuneate field defect extending from the blindspot to the raphe or to the periphery of the field has always been regarded as an important differential point in the diagnosis of juxtapapillary choroiditis (Traquair, Jensen and Abraham). However, if the field is plotted for the usual type of acute exudative choroiditis (not adjacent to the disk), the defect is of the same type but truncated, as mentioned

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by Traquair.[1] In other words, a nerve bundle defect is obtained which involves the nerve fibers passing over the lesion from the lesion to the final destination of those nerve fibers. Partial arcuate or partial cuneate defects result. Thus, the differences between the field defects of acute exudative and acute juxtapapillary choroiditis are quantitative rather than qualitative.

I wish to consider Jensen's disease as a clinical variant of acute exudative choroiditis. I think that the mechanism of production, the basic pathologic process and the pathologic physiology, is the same for both conditions and that any conclusions regarding causation or therapy apply equally well to both types.

HISTORY AND EXAMINATION

Acute choroiditis occurrs principally in young adults who are usually in good physical condition. There is often a history of an antecedent cold in the head or sinusitis, and the disease usually occurs during the late winter or early spring months. It has occurred during lactation. In many instances no apparent cause can be found.

The usual routine diagnostic procedure includes a search for foci of infection, a general physical examination, a Mantoux or subcutaneous tuberculin test, a Wassermann test of the blood, roentgenograms of the chest, sinuses and teeth and any other tests that come to mind. The results of such examinations are usually woefully inadequate as far as furthering knowledge of the causation of the ocular lesion is concerned.

THERAPY

Among the various treatments used for acute exudative choroiditis are rest in bed, the injection of vaccines and foreign protein, diathermy, fever therapy, the administration of sulfanilamide, removal of known or questionable foci of infection, prostatic massage, the induction of sweats and, last but not least, the injection of tuberculin.

Adjuvant and local therapy include the administration of vitamins, tonics, calcium, atropine and ethylmorphine hydrochloride and subconjunctival injections of salt solution. Many different therapeutic procedures are often used for each individual case, so that if improvement does occur it is impossible to decide which drug or type of therapy deserves credit.

A disease for which there are many different types of treatment is a disease the causation and pathologic physiology of which are unknown. There is no question concerning the value of arsphenamine in syphilis, of quinine in malaria or of antitoxins and antiserums for

1. Traquair, H. M.: An Introduction to Clinical Perimetry, ed. 2, London, Henry Kimpton, 1931, pp. 95-97.

certain specific bacterial infections. There is more than a reasonable doubt as to the efficacy of any of the drugs or therapeutic procedures used for acute choroiditis. If any therapy is of definite value in the treatment of a particular disease, it does not require years of use to establish its worth. The various therapeutic procedures used for acute exudative choroiditis have been in use for many years. There is, even now, no unanimity of opinion as to their real worth.

With the time-honored methods of treatment, months are usually required for cure (?). Without any treatment the lesion heals in several months, leaving the typical pigmented, atrophic chorioretinal patch.

In my opinion many of the customary therapeutic measures deter healing, and some are potentially dangerous. Death has followed fever therapy; injections of foreign protein are not entirely free from danger; the complications and deaths which have been reported following the use of sulfanilamide have attained large proportions. Acute exudative choroiditis is a self-limited disease which does not endanger life or cause any of the complications known to follow the use of the aforementioned types of therapy. No treatment can be justified which exposes the patient to greater hazards of life, limbs or comfort than the disease itself does.

CAUSATION

At the present time I do not wish to discuss at length the causation of acute choroiditis. Tuberculosis is rarely, if ever, a cause. In many cases an acute infection of the upper part of the respiratory tract seems to bear a casual relation to the attack. Focal infection may play a part in some cases. There seem to be a number of extrinsic predisposing factors. An intrinsic factor which determines the site and extent of the lesion is probably of fundamental importance. The acute choroidal lesion is a general type of reaction resulting from one or several causes.

SIMILARITY OF ACUTE CHOROIDITIS TO OTHER ACUTE OCULAR REACTIONS

In acute exudative choroiditis the onset is strikingly similar to that of acute spastic closure of the central retinal artery and acute retrobulbar neuritis. The onset of all three conditions is sudden; each condition attains its acme in a few hours and if untreated it slowly resolves in weeks or months. The final result is an atrophic area in the choroid, retina or optic nerve, with more or less loss of visual function.

In acute spastic closure of the central retinal artery (or one of its branches) the spasm can be seen. There is intense edema of the retina, the veins are engorged and there are sometimes small hemorrhages.

In acute retrobulbar neuritis spasm of a small arteriole in the optic nerve is accompanied by an intense edema of the adjacent nerve, so

that all of the fibers may be temporarily unable to conduct impulses. There is also round cell infiltration. The favorable response of this lesion to intensive vasodilator therapy admits of no other interpretation than that the fundamental pathologic process is an acute localized arteriolar spasm with increased capillary permeability.

To show that the idea of a primary vascular origin for acute exudative choroiditis is not new, a statement by Moore [2] may be of interest. Regarding these cases, Moore said:

> . . . minute emboli occur in the blood stream of individuals in health. . . . Should such an embolus . . . lodge in any of the intraocular vessels, whether those of the retina or choroid, the resulting obscuration of vision cannot be overlooked. . . . Such an occurrence in the retinal artery is well recognized under the term "embolism of the central retinal artery" and it is significant that in many or most such cases no source of the embolus is discovered, and I suggest that many of the cases of choroidal lesions which by some are attributed to the tubercle bacillus are in fact brought about by the lodgement of an embolus of unknown source in one of the vessels of the choroid.

The foregoing statement was written in 1925. If it is recalled that today it is the general consensus among many ophthalmologists that sudden closure of the central retinal artery is usually due to spasm rather than to embolism, it is evident that Moore's statement sums up the similarity between acute closure of the central retinal artery and acute choroiditis.

In acute exudative choroiditis the white elevated patch is due to an area of localized edema in the choroid. As the lesion heals, the final atrophic area is always smaller than the original acute lesion. Sections through a healed lesion show one or two narrowed or obliterated choroidal arterioles with thickened walls, obliteration of the overlying choriocapillaries and more or less atrophy of the overlying retina. This is well pictured in Troncoso's and in Thiel's atlas.

Histologic examination of an eye enucleated sixty-six days after the onset of a juxtapapillary choroiditis was reported by Abraham.[3] There was a hemorrhagic coagulum between the choroid and the retina, with congestion and necrosis of the nerve fiber and ganglion cell layers of the retina and hemorrhage and granulation tissue in the outer retinal layers. The choroid was extensively necrotic in many areas. There was also an extensive lymphocytic infiltration around the plexus of short ciliary vessels (circle of Zinn). The choroidal arterioles were not described. Abraham concluded that ". . . the condition is a

2. Moore, R. F.: Medical Ophthalmology, ed. 2, London, J. & A. Churchill, 1925, pp. 243-245.

3. Abraham, S. V.: Chorioretinitis Juxtapapillaris (Jensen), Arch. Ophth. 8:503 (Oct.) 1932.

chronic inflammatory process primarily in the choroid and involving the plexus of vessels forming the circle of Zinn."

In an earlier article on Jensen's disease, Abraham [4] stated:

> While awaiting more information as to the etiology and histologic observations, one can therefore only say that retinochoroiditis juxtapapillaris is a local inflammatory condition of a toxic or infectious nature with involvement of the retinal [choroidal (?) W. F. D.] blood vessels and a small group of nerve fibers in the anterior part of the vagina nervus opticus.

Among the cases of acute juxtapapillary choroiditis which have been reported in the literature, the following are of interest. In Abraham's [3] case one eye became steadily worse for sixty-six days and was then enucleated; two attacks in the other eye cleared in four and one-half weeks and six months, respectively.

Statti's [5] patient, whom I had the opportunity of observing, recovered normal vision in six months. No treatment was given, and the only abnormal finding was a cloudy right antrum. Bossalino [6] reported 5 cases. In 1 case three months were required for healing; in the other 4 cases all active symptoms subsided within five months. Tuberculin tests were positive in 2 cases, and the condition was considered as possibly due to tuberculosis in the other 3 cases.

It is apparent that the usual modes of treatment are about as effective as no treatment. A new point of view, a reinterpretation of the gross and microscopic observations and a new therapeutic approach, based on the pathologic physiology, would seem to be justified.

PATHOLOGIC PHYSIOLOGY OF ACUTE CHOROIDITIS

The basic pathologic process is identical for acute exudative choroiditis, acute spastic closure of the central retinal artery and acute retrobulbar neuritis. This process consists of arteriolar spasm, capillary dilatation and increased capillary permeability with transudation of plasma, white cells and, in severe cases, erythrocytes. Ricker has called these three stages prestasis, peristasis and stasis, or liquor stasis, leukostasis and rubrostasis, depending on the type of transudate or exudate. This picture will vary, depending on the anatomic structure of the involved tissue, but the differences seen from tissue to tissue and from lesion to lesion are quantitative rather than qualitative. The result is anoxia of the tissues.

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4. Abraham, S. V.: Retinochoroiditis Juxtapapillaris—Jensen, Arch. Ophth. **2**:452 (Oct.) 1929.

5. Statti, L. W.: Retinitis Juxtapapillaris, Arch. Ophth. **9**:947 (June) 1933.

6. Bossalino, G.: Retino-coroidite di Edmund Jensen, Arch. di ottal. **43**:1 (Jan.-Feb.) 1936; abstracted, Arch. Ophth. **17**:173 (Jan.) 1937.

A factor which determines the location of a lesion in the choroid, optic nerve or retina is undoubtedly an increased sensitivity of the smooth muscle in the arteriolar wall to some substance in the circulating blood. The recurrence of similar lesions in the same person would seem to indicate that this vascular hypersensitivity is of fundamental importance in any study of the causation of acute choroiditis or the other pathologically similar lesions. On this basis, it is understandable that the same chemical agent can cause different lesions in different persons.

In my opinion this chemical agent is histamine, a histamine-like compound or a histamine-colloid compound, because histamine is the only substance occurring normally in the body which can cause arteriolar constriction and capillary dilatation with increased capillary permeability. Lack of oxygen has a similar action on the capillaries, and large amounts of epinephrine injected intravenously can give the same pathologic picture, the capillary changes being ascribed to the anoxia resulting from the intense vasoconstriction.

Peters and Van Slyke [7] stated: ". . . Dale, Abel and their associates have shown that it [histamine] is not only highly toxic, but that it has, in minute amounts, such effects . . . on the contractility of smooth muscle and on capillaries that it may, perhaps, be classed with the hormones." And, as Horder [8] recently said: ". . . What was disease but a state of morbid physiology? The functions by which a man lived in health were the same as those through which he expressed his pathologic state. . . ."

If acute choroiditis is due to arteriolar spasm with a resulting increased dilatation and permeability of the capillaries, the condition should improve with intensive vasodilator therapy. If the response to this type of treatment is better than that resulting from the customary therapeutic measures and better than that without treatment, this interpretation of the pathologic physiology of acute choroiditis deserves serious consideration. As Moon [9] has recently said: ". . . many phenomena called toxic are essentially anoxic."

The purpose of vasodilator therapy is to improve the blood supply to the tissues, thereby relieving the anoxia of the tissues.

REPORT OF CASES

Recently, I have treated 5 patients with acute exudative choroiditis with only intravenous injections of sodium nitrite. The choroiditis in 3 of the cases was of the juxtapapillary type.

7. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1931, vol. 1.

8. Horder: The Approach to Medicine, Brit. M. J. 1:632 (March 25) 1939.

9. Moon, V. H.: Shock and Related Capillary Phenomena, New York, Oxford University Press, 1938.

CASE 1.—D. G., a youth of 18, was seen on Aug. 4, 1938, with the history of loss of sight in the right eye for eight days. The past history was unimportant except for the fact that he had been bathing in the ocean one week prior to the loss of sight and had felt weak and fatigued after coming out of the water.

Vision in the right eye was 20/30—; the media were clear, and there was juxtapapillary choroiditis at the lower and outer margin of the disk. The lower pole of the disk was concealed by the edema. The lesion was elevated 2 diopters, and the retinal edema extended almost up to the macula. The inferior temporal vein was markedly engorged, and there were a few small retinal hemorrhages. In the nasal periphery of the fundus were several old pigmented choroidal lesions. Examination of the visual field showed an arcuate defect in the upper field.

Starting on August 4, the patient received fourteen daily intravenous injections of sodium nitrite (0.1 Gm.). On August 8 the field defect was smaller, the vision was 20/30, the lower pole of the disk was visible and the choroidal lesion was much smaller and flatter. On August 14 the vision was 20/20—, the field was better, the hemorrhages had disappeared, there was no engorgement of the inferior temporal vein and the choroidal lesion was visible as only a small subretinal area of edema. On August 18 the site of the choroidal lesion was barely perceptible. When the patient was last seen on October 7, the vision was 20/20, the field showed only a small scotoma connected with the blindspot and the fundus was normal except for a round area of choroidal atrophy one-tenth the diameter of the disk and separated from the disk by a distance equal to the diameter of the lesion.

The patient received fourteen intravenous injections of sodium nitrite. There was marked improvement in the lesion after four days. Vision improved from 20/30— to 20/20— in nine days. The fundus was almost normal in fourteen days. The field defect continued to decrease in size for two months.

CASE 2.—C. B., a woman of 23, was seen on Nov. 7, 1938, with the complaint of loss of sight in the left eye, discovered on awakening on November 2. The past history was unimportant except for the fact that the tonsils were being removed by electrocoagulation. A Mantoux test (done in January 1939) gave a negative reaction.

Vision in the left eye was 8/200, the media were clear and there was juxtapapillary choroiditis under the inferior temporal vessels. The lesion was similar to that described in case 1, except that there were no hemorrhages in the retina and the lower pole of the disk was only slightly obscured by edema. The field[10] showed a large nerve fiber bundle defect extending to the horizontal raphe.

Beginning on November 7, the patient received twelve daily intravenous injections of sodium nitrite (0.1 Gm.). On November 11 the vision was 20/70—; the choroidal lesion was smaller and more sharply circumscribed, with less edema around it. On November 28 the vision was 20/40—, the field defect was much smaller and the fundus showed only a small, white, slightly elevated patch under the inferior temporal artery and about twice the diameter of the artery, nearly 1 disk diameter away from the disk.

The patient was seen next on Jan. 11, 1939. The vision was 20/20, and the examination of the fundus showed a small white spot less than one-sixteenth the diameter of the disk under the inferior temporal artery. The field taken on January 15 showed a small absolute arcuate scotoma, which was indistinguishable

10. The fields in this case have been described in case 5 in a paper by W. F. Duggan on Tangent Screen Scotometry: Value in Diagnosis, Prognosis and Evaluation of Therapy (Arch. Ophth. **23**:316 [Feb. 5] 1940).

from that found in chronic glaucoma. The patient stated that her vision had been normal for at least one month.

The patient received twelve injections of sodium nitrite. After four days there was definite improvement in the vision and in the lesion of the fundus. After twenty-one days the vision was 20/40—, and the lesion of the fundus was practically healed. During the next six weeks vision improved to 20/20.

CASE 3.—L. T., an Italian man of 34, was seen on Feb. 8, 1939, with the history of loss of sight in the left eye for three weeks. After the onset of visual loss he was ill for a few days with a severe cold in the head. Several years before he had had a similar attack in the same eye, which eventually cleared without treatment.

Vision in the left eye was 20/100. The anterior segment of the eye was normal. There was a diffuse haze in the vitreous which prevented a clear view of the fundus. In the lower nasal quadrant of the fundus there were several scattered heavily pigmented old choroidal lesions. In the midst of these there was an elongated white patch of acute choroiditis elevated 3 or 4 diopters. The field showed a truncated defect in the upper temporal part. The right eye was normal.

Between February 8 and February 22 the patient received fourteen intravenous injections of sodium nitrite (0.1 Gm.), after which he took ½ grain (0.032 Gm.) of erythrityl tetranitrate twice daily for a week.

On February 13 (after the sixth injection) the vision had improved to 20/50 + 1, the vitreous was clearer and the choroidal lesion was smaller and less elevated. On February 20 (after twelve injections) the vision was 20/30—, the vitreous was still clearer and the choroidal lesion was flat. On February 27 the vision was 20/20—2, the vitreous was clear and only a faint whitish haze indicated the site of the original lesion. On April 19 the region of the lesion was visible only as an area of depigmentation, and the vision was 20/20—2.

Roentgenograms showed evidences of bilateral frontal, ethmoid and maxillary sinusitis. The right antrum was irrigated on April 17; the return fluid was clear.

The patient received fourteen intravenous injections of sodium nitrite. There was definite improvement in the vision, the lesion of the fundus and the appearance of the vitreous after the sixth injection. Nineteen days after treatment was started the vision was 20/20—2, the choroidal lesion was barely visible and there was marked improvement in the appearance of the vitreous.

CASE 4.—M. T., a Negro man of 23, was seen on March 29, 1939, with the complaint of loss of sight in the right eye of three days' duration. The vision was 20/40; there was a defect in the whole upper field, and examination of the fundus revealed marked juxtapapillary choroiditis at the lower temporal side of the disk, with elevation of the lesion, many hemorrhages and edema of the retina below the lesion. Later, the patient was seen to have a closure of the inferior retinal arteries. He was given thirteen daily injections of sodium nitrite. The vision improved to 20/20 after six injections, and the field above the fixation point improved slightly. After one month there was only a slight improvement in the fundus picture.

I think that in this case the choroidal and retinal pathologic process was so severe and the vascular supply so impaired that vasodilator therapy probably did not materially improve the condition.

The Wassermann and Mantoux tests were negative.

CASE 5.—M. S., a woman of 50, was seen on May 3, 1939, with the complaint of blurred vision in the right eye for two weeks. The vision was 20/100, there

were heavy opacities of the vitreous, the optic disk was barely visible and there were an old pigmented choroidal lesion several disk diameters below the disk, a large fresh patch of acute exudative choroiditis in the lower periphery of the fundus and a corresponding contraction of the field, up and out. The patient had had two previous attacks of choroiditis, and no foci of infection had been discovered.

Daily intravenous injections of sodium nitrite were given. On May 12, after nine injections, the vision was 20/30—, the vitreous was definitely clearer, the area of acute choroiditis had decreased to about half its former size and the optic disk was easily seen.

Five more injections of the sodium nitrite were given, followed by the oral administration of erythrityl tetranitrate (30 mg.) each night for two weeks. As the choroidal lesion decreased in size, pigment was visible in the retina, and it was obvious that the new lesion had been directly adjacent to an older lesion. On June 1, in the lower periphery of the retina one could see a small white area of old choroiditis (from an earlier attack) with pigment on its temporal border, and lateral to the pigment there was an area of depigmentation corresponding to the area involved in the last attack. The patient was seen last on June 9; the vision was still 20/30—, there were some old opacities in the vitreous and the disk was clearly visible.

As the vision had been 20/30 for the year preceding this last attack, one may assume that the patient had regained most of the vision she had had prior to this attack.

The patient received fourteen injections of sodium nitrite. After nine days of treatment the vision improved from 20/100 to 20/30—; there was a marked decrease in the cloudiness of the vitreous, and the area of acute choroiditis had decreased to about one-half its original size. Six days later the area of acute edema had completely disappeared. Twenty-nine days after the onset of the treatment an area of depigmentation represented the site of the original acute lesion.

SUMMARY AND CONCLUSIONS

The general characteristics of acute exudative choroiditis have been briefly reviewed. The juxtapapillary type differs from the usual type only because of its location adjacent to the optic disk. There are no fundamental differences between these two varieties.

The causation of this condition has been ascribed to focal infection, to tuberculosis and to an undetermined bacterial source. All theories assume that it is toxic.

There are many different therapeutic procedures in vogue. None are particularly effective, and there is no unanimity of opinion as to their value.

The usual time required for healing of the lesion, with or without treatment, varies between five weeks and seven months; in most cases more than three months is required. Some types of therapy probably delay healing; a few are potentially dangerous.

Acute choroiditis seems to be due to a localized arteriolar spasm with increased capillary permeability which results in transudation of

plasma, white cells and occasionally erythrocytes. The same clinicopathologic picture also occurs in acute retrobulbar neuritis and in acute spastic closure of the central retinal artery or one of its branches. This typical pathologic process, common to three apparently unrelated conditions, is the result of an acute vascular catastrophe and causes acute anoxia of the tissues.

General and special examinations often give negative results, because localized anoxia of the tissues can exist without anoxemia.

Histamine (which occurs normally in the body in small amounts) or histamine-like bodies are suggested as the agent causing this acute vascular catastrophe and the resulting anoxia of the tissues. This hypothesis explains the frequent occurrence of this condition in cold weather and also explains the cases in which the condition is attributed to focal infection.

While foci of infection and colds in the head may be a contributing factor in the development of acute choroiditis, something more than treatment of these conditions is necessary. Known foci of infection should be removed on general principles. Subjecting the patient to a barrage of operations is not good therapy. There seems to be no logical basis for prescribing debilitating treatments.

Acute localized arteriolar spasm can cause capillary dilatation, increased capillary permeability and transudation of plasma and cells, with resulting anoxia of the tissues. Treatment directed toward relieving this arteriolar spasm has a sound physiologic and pathologic basis. None of the time-honored methods of treatment have this basis, none are particularly effective and some may delay healing, because they often cause in other organs the same basic pathologic process which is found in acute choroiditis.

Five cases of acute exudative choroiditis are reported in which vasodilator therapy only was used. The condition in 1 case (case 4) was essentially unaffected by this therapy. The patient in case 1 attained normal vision and a nearly normal fundus in fourteen days. The vision in case 2 improved from 8/200 to 20/40— in twenty-one days, and the choroidal lesion was barely perceptible. Sometime during the next six weeks the vision improved to 20/20. The vision in case 3 improved from 20/100 to 20/20—2 in nineteen days, and the lesion was barely perceptible at this time. In these 3 cases pigment did not develop around the lesion during healing. Vision in case 5 improved from 20/100 to 20/30— in nine days, and the lesion had decreased to about half its original size. Six days later the acute lesion had completely disappeared.

In no case was operation performed. No foci of infection were treated. Neither vaccines nor foreign protein therapy was used. Tuberculin was not used, nor was any patient hospitalized. Even mydriatics

were not used except for the purpose of examining the fundi. The treatment is simple, inexpensive and safe. Moreover, the use of vasodilators for the treatment of this condition has a sound physiologic and pathologic basis.

NOTE.—At the time this paper was read a comprehensive article on solitary retinochoroiditis by Christopher Heath appeared in the *British Journal of Ophthalmology*.[11] He mentioned the lack of evidence for tuberculosis as a cause for this condition, the absence of even questionable foci of infection in many cases and the presence of spasms of branches of the retinal arteries in 4 of his 24 cases. Heath has not been impressed by the therapy customarily used for this condition; he stated that "there is no good evidence that tuberculin injections ameliorate or shorten the course of the attack."

11. Heath, C.: Solitary Retino-Choroiditis with Reference to Retino-Choroiditis Juxtapapillaris—Jensen, Brit. J. Ophth. **23**:289 (May) 1939.

NEW METHOD OF SUBJECTIVE REFRACTION INVOLVING IDENTICAL TECHNICS IN STATIC AND IN DYNAMIC TESTS

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The technics and data which are presented here are those which follow from the specific introduction of brightness-contrast as a criterion of visibility into certain phases of subjective refraction. This criterion is not only a fundamental one in physiologic optics but a unique one from the point of view of refraction, since it permits the functioning of convergence in the absence of a stimulus for relative accommodation. Furthermore, the procedures for determining the refractive states of the eyes at the near point are precisely the same as those used for determining the refractive states at the far point. Although the clinical data presented are exploratory rather than conclusive, the results obtained suggest certain new concepts related to the functioning of the mechanisms of accommodation. They also suggest diagnoses of certain conditions which have been difficult when considered from the usual tenets of ocular examination.

VISUAL THRESHOLDS AND VISIBILITY

Throughout this discussion the term visibility is used to denote the intensity of a psychophysical stimulus which evokes visual perception and discrimination. By definition, this quantity depends not only on the external physical characteristics of the stimulus but on the efficacy of the visual processes of the observer. However, if it is specified that all measurements of visibility are to be made with the same test object and under the same environment, the term visibility refers directly to the visual efficacy of the observer. If an object is visible, it is necessary but not sufficient that the size of the object, its contrast with its background, the brightness of the background and the duration of the image on the retina each exceed certain liminal values.[1] Thus there are at least four fundamental variables of the threshold stimulus which may be used as criteria for the quantitative appraisal of visibility and, therefore, of visual efficiency.

From the Lighting Research Laboratory, General Electric Company.

1. Cobb, P. W., and Moss, F. K.: The Four Variables of the Visual Threshold, J. Franklin Inst. **205**:831, 1928.

With the usual subjective procedures, a change in refraction is correlated with a change in the size of the threshold stimulus. While such procedures are convenient in clinical practice, they do not possess greater fundamental significance [2] than some other procedure which involves another variable of the threshold stimulus as a criterion. With the Snellen chart, for example, threshold conditions are obtained by varying the size of the test characters while the factors of contrast and brightness remain constant so far as the latter are fixed by the chart itself. However, it should be obvious that these test objects represent but one series (maximal contrast) of an infinite number of series of test objects differing in contrast and brightness which might be used for the purposes of refraction. In our procedures the size and configuration of a single test object remain constant while its contrast and brightness are simultaneously varied in order to reduce it to threshold visibility.

SENSITOMETRIC PROCEDURES

The quantitative appraisal of visibility by means of photometric criteria is here designated as sensitometry in order to distinguish the method from the usual subjective procedures involving the criterion of threshold size. The sensitometric method also differs fundamentally from other methods for obtaining threshold conditions in that changes in the visual stimulus are made by placing gradient filters before the eyes rather than by altering the physical characteristics of the test object itself. Thus the visibility of all objects in the entire binocular field is controlled with the sensitometric procedures. It will be shown that this attribute of the sensitometric method is essential to the inhibition of accommodation—a basically important characteristic of the method.

General Procedure.—Brightness-contrast thresholds may be obtained by placing gradient filters directly in front of the eyes and altering the density of these filters, or wedges (by rotation), until the test object located at some near point or at distance is barely perceived. The visibility of the test object under these conditions is then read directly from a scale associated with the circular gradient filters (fig. 1), which is previously calibrated in terms of visibility. This process is repeated with trial lenses of various powers placed successively before the eyes.

At the beginning of each measurement all details of the entire visual field except a bright but vaguely defined convergence target (fig. 2) are veiled by the filters, and as the density of these filters is gradually reduced the test object emerges from the obscurity of the diffuse luminous field. Until this condition is reached, it follows that there

2. Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, C. V. Mosby Company, 1934.

can be no stimulus for accommodative action. After the threshold is reached, no further changes are made by the subject in the position of the gradient filters before his eyes, and hence any changes in accommodation which may occur after the test object is first seen do not affect the measurement of visibility. Since a stimulus for accommodation is thus avoided during the process of measurement, the ability of the

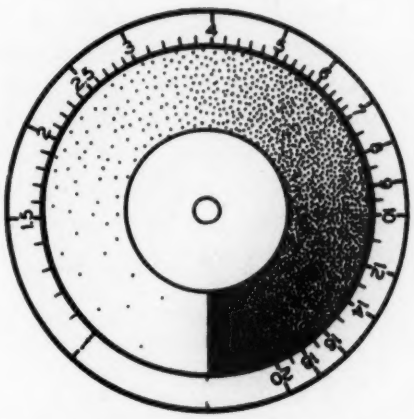

Fig. 1.—One of the two gradient filters of the Luckiesh-Moss sensitometer and its associated scale of relative visibility.

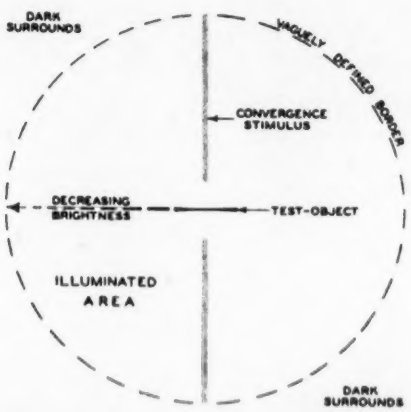

Fig. 2.—The test object, convergence target and the visual field as presented by sensitometric study.

subject to see the test object increases as refractive errors are progressively corrected and reaches a maximum when the image of the test object is focused exactly on the retina. The plotting of the data obtained with various trial lenses results in a graph similar to those shown in figure 3.

The Avoidance of Accommodation.—It has been shown elsewhere [3] that accommodation is preventable through the avoidance of an adequate stimulus for this function. This does not appear to be possible with the usual objects and procedures used to test visual acuity, since as the threshold of resolution is approached the critical details of the object gradually become unrecognizable, although the object as a whole may still readily be perceived. Thus sufficient stimulation may be received under these conditions to induce some degree of accommodation. With the sensitometric method, the test object is brought from a subthreshold

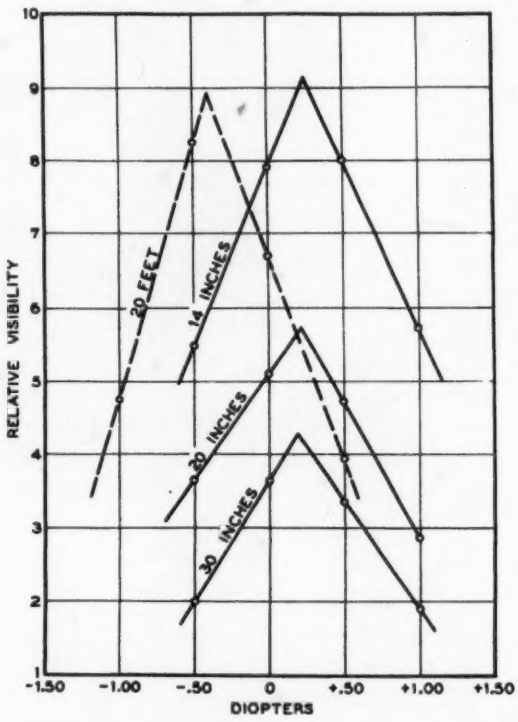

Fig. 3.—Relations between visibility and refraction for various fixation distances as determined for a typical subject.

condition to the threshold of visibility by gradually increasing its contrast and brightness, while the critical details of all other objects remain invisible. Hence there is no physical stimulus for accommodation until the lowest threshold of visibility, involving the mere recognition of the presence of the test object, has been reached.

3. Luckiesh, M., and Moss, F. K.: The Avoidance of Dynamic Accommodation Through the Use of a Brightness-Contrast Threshold, Am. J. Ophth. **20**: 469, 1937.

The avoidance of accommodation to the trial lenses through the use of absorbing and diffusing filters before the eyes is experimentally confirmed by the data in table 1 and figure 3.

It will be noted that the average decrements in visibility resulting from overcorrection and undercorrection of 0.50 diopters, respectively, are about equal, thus denoting a symmetric relation between visibility and refraction. Data of this character are obtained by the sensitometric method under both static and dynamic conditions. Obviously, if relative accommodation were stimulated by the trial lenses or by other factors, not even approximate symmetry would be obtained. Thus symmetry of the visibility-refraction relation is taken as a critical indication of the control of accommodation with the sensitometric procedures.

The Stimulation of Convergence.—Since the demand for single binocular vision is a most emphatic one, it is axiomatic that a binocular stimulus for convergence is a desirable characteristic of any method

TABLE 1.—*Average Percentages of Maximal Visibility Obtained with Corrections of 0.50 Diopter, Plus and Minus, Added to the Power Producing Maximal Visibility* *

Left Eye				Right Eye			
Meridian of Best Vision		Meridian of Poorest Vision		Meridian of Best Vision		Meridian of Poorest Vision	
+	−	+	−	+	−	+	−
77	78	75	76	75	78	75	78

* The data for the 10 individual subjects on which this average is based are presented elsewhere.[3]

of subjective refraction. In conformity with this and with other obvious considerations, the sensitometric method involves a separate fixation target (fig. 2) in the plane of the test object, and this target is viewed binocularly during the monocular examination of the refractive states of the eyes. In the absence of an adequate stimulus for accommodation, convergence becomes the controlling factor in the physiologic situation established by the sensitometric procedures, while the excess or deficiency of the refraction is the measured quantity. Thus the procedures of sensitometry are in accord with the principle that harmony between accommodation and convergence is to be obtained by changing the demand on accommodation rather than by interfering with convergence.[4]

Under these conditions it may be assumed that the relation between accommodation and convergence established by and maintained during the sensitometric examination is a natural and a comfortable one for the subject, since the accommodative states are those induced by the

4. Laurance, L.: Visual Optics and Sight Testing, London, The School of Optics, Ltd., 1926.

associated innervation of the extrinsic and intrinsic muscles. Thus the spherical lenses prescribed from such procedures should not require either positive or negative relative accommodation.

The convergence target, consisting of a vaguely defined vertical band of diffused light, is located in the plane of the test object and at right angles to the longitudinal axis of the latter, as is illustrated in figure 2. This relatively bright band of diffuse light (the light is diffused at the source and also by the filters of the sensitometer) provides an adequate stimulus for convergence and (as will be shown later) an inadequate one for accommodation. This assumption is in qualitative agreement with the statement of Sheard [5] that "light and color, *per se,* as obtained by the use of filtered radiation for fixation objects, supplies but little, if any, stimulus for accommodative action." If cylindric trial lenses are used in determining the visibility-refraction relation, it is obvious that the visibility of the test object may be altered without appreciably changing that of the convergence target, since the axes of the lenses are at right angles with the vertical band of light comprising the target. Furthermore, the visibility of the latter is far above the threshold under all conditions imposed by the trial lenses or the filters of the sensitometer.

The Sensitometer.—Our instrument, as illustrated in figure 4, consists essentially of two colorless circular photographic gradient filters (fig. 1), precise in optical density and diffusion, which may be rotated simultaneously in front of the eyes of the subject while the latter fixates the convergence target. These gradient filters not only alter the apparent brightness of the visual field due to absorption but also alter the contrast of objects within the visual field due to the slightly diffusing character (Q factor in photography) of the photographic filters. This component of the ensemble shown in figure 1 is essentially the Luckiesh-Moss visibility meter, and it could be incorporated as a simple addition to the usual phoropter. The construction, calibration, operation and precision of the visibility meter have been described in detail elsewhere.[6]

The Test Object.—The single test object used for sensitometry examination under both dynamic and static [7] conditions is illustrated in figure 5. In general, the shape of this object is such that its visibility, under threshold conditions, is uniform throughout its longitudinal dimension. The latter characteristic reduces substantially the extent of the threshold "region" and thus adds to the precision of the sensitometric

5. Sheard, C.: Physiological Optics, in Wood, C. A.: American Encyclopedia and Dictionary of Ophthalmology, Chicago, Cleveland Press, 1918, vol. 13, pp. 9720-10214.

6. Luckiesh, M., and Moss, F. K.: The Science of Seeing, New York, D. Van Nostrand Company, Inc., 1937.

7. These terms merely indicate the distance of the test object from the subject.

measurements. The test object used in both our procedures is 60 minutes in length and 1.5 and 3.75 minutes in width at its center and extremities, respectively. Thus its length is approximately equal to the diameter of the average fovea. Under the brightness conditions which prevail during our measurements, this object when viewed with the naked eyes presents the same order of visibility as the 20/200 characters on the Snellen chart. Since the threshold conditions are obtained by photometric changes in the stimulus, the measurements may be repeated any number of times without involving distortions due to memory, thus permitting the attainment of a high degree of precision.

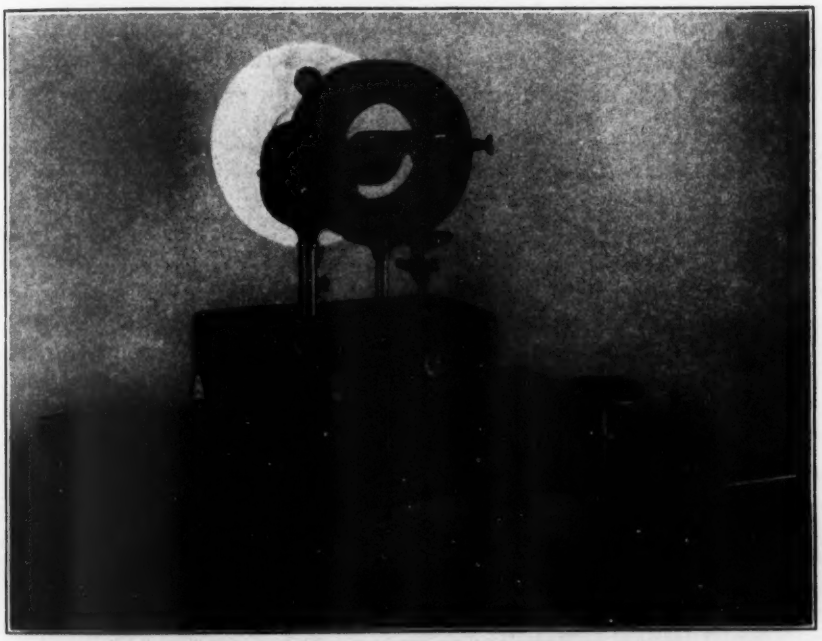

Fig. 4.—The laboratory model of the Luckiesh-Moss sensitometer used in the present investigation.

Fig. 5.—The biconcave test object used for both static and dynamic sensitometric examination.

The biconcave test object is located at the center of an extended white screen, which may be placed at any desired distance from the subject. The screen is illuminated in such a manner that the brightness of the illuminated (and more or less circular) area gradually diminishes toward its periphery, as is indicated by figure 2. Furthermore, the brightness relations in the entire visual field are so regulated that only the con-

vergence target is seen through the visibility meter until after the test object has become visible. In other words, the visibility of all other details of the visual field except the vaguely defined convergence target is reduced below the threshold by the filters, definite stimuli for accommodation thus being avoided.

Clinical Procedures.—For simplicity in describing the detailed procedures of sensitometry, it will be assumed that the method is to be used to determine the spherical power required to obtain maximal visibility under dynamic conditions. In general, the sensitometric procedures are considered as supplements rather than as substitutes for certain usual tests. However, the sensitometric method does not depend on data obtained by other test methods, nor is it necessary that the method be restricted to the spherical component of the ophthalmic prescription. The essential steps in the procedures are as follows:

1. A convex cylindric lens of about 2.5 diopters is placed before one eye with its axis horizontal. The purpose of this lens is to obliterate the image of the horizontal bar test object and thus confine the refraction to the other eye.

2. Spherical or cylindric lenses of + 1.00, + 0.50, — 0.50 and — 1.00 diopter, respectively, are successively placed before the eye under examination, and several measurements of the visibility of the test object are made with each of these lenses. These measurements are made invariably by approaching the threshold of visibility from a subliminal condition. The reasons for selecting these particular trial lenses (in the assumed case of emmetropia) will be obvious from figure 3. In any case, the powers of the trial lenses should similarly "bracket" the correction producing maximal visibility.

3. The average visibilities obtained with each trial lens are plotted as shown in figure 3, and straight lines are drawn through these points. The latter procedure is justifiable, since it has been adequately established that the relation between visibility and refraction is a linear one. This is due to the characteristics of the particular scale of visibility associated with the gradient filters. The resultant graph should be symmetric about the axis of maximal visibility, thus indicating the avoidance of accommodation. Its apex indicates the correction which will produce maximal visibility without the exercise of relative accommodation.

4. The correction producing maximal visibility may also be determined from three series of measurements indicated by points *1*, *2* and *3* in figure 6. Thus points *1* and *2* determine the relation between refraction and visibility; and the average refraction, *M*, indicated by the bisector of the line joining points of equal visibility on the "positive" and "negative" branches of the visibility-refraction relation, corresponds to that yielding maximal visibility.

DYNAMIC SENSITOMETRIC EXAMINATION

Clinical Data.—An experimental group of 20 subjects, including both men and women, were selected at random from technical and clerical groups. They varied in age from about 25 to 35 years. Among these subjects were included 8 persons who had never worn glasses. In regard to the latter, all that can be said with certainty is that if

refractive errors had been involved they were not introspectively objectionable enough to induce the wearing of glasses.

All data presented in table 2 were obtained with the subjects wearing their habitual corrections, if any. Hence these dioptric values indicate the additional powers required by the individual subjects in order to obtain maximal visibility at a fixation distance of 16 inches (40 cm.). These values were obtained from approximately symmetric relations between visibility and refraction, thus indicating that the inherent interlocking between accommodation and convergence was not

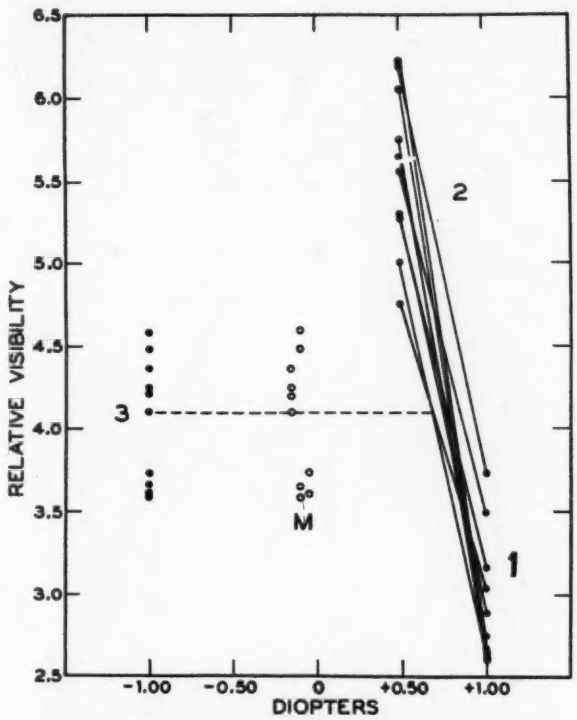

Fig. 6.—The data obtained for a typical emmetropic subject at ten successive examinations and represented by the "3 point" method of plotting.

disturbed by the procedures of dynamic sensitometry. In interpreting these data, it is to be recalled that the test object for the sensitometric examination consists of a narrow elongated bar, and hence the data refer to the refraction of a restricted foveal region. For present purposes, it is tacitly assumed that astigmatism was properly corrected by the eyeglasses worn by the subjects.

Data Obtained by Dynamic Sensitometric Examination.—Considering the 20 subjects as a group, it will be noted from table 2 that the "average" correction prescribed from numerous static and dynamic tests and

modified by the clinical experience of the ophthalmologist is about the same as that indicated directly by dynamic sensitometric examination. As a matter of fact, these data confirm the correctness of the "average" refraction to a degree which would scarcely be claimed by the most skilled refractionist. It will also be noted that there is no indication of a lag of accommodation [8] when all stimuli for accommodation are eliminated.

TABLE 2.—*Dioptric Values Required for Maximal Visibility in Addition to the Usual Corrections Worn, if Any* *

Subject	O. D.	O. S.	O. D. — O. S.	Subject	O. D.	O. S.	O. D. — O. S.
1†	−0.40	+0.10	−0.50	11‡	0	0	0
	−0.40	+0.05	−0.45		0	−0.25	+0.25
2	+0.10	+0.25	−0.15	12	0	−0.05	+0.05
	+0.15	+0.15	0		0	0	0
3‡	+0.10	+0.10	0	13‡	+0.05	−0.15	+0.20
	−0.05	−0.05	0		+0.05	−0.10	+0.15
4	+0.20	0	+0.20	14‡	−0.05	+0.50	−0.55
	+0.40	+0.20	+0.20		0	+0.45	−0.45
5	+0.35	0	+0.35	15	+0.20	−0.05	+0.25
	+0.30	+0.15	+0.15		+0.10	−0.10	+0.20
6‡	0	0	0	16	+0.05	+0.20	−0.15
	−0.25	−0.05	−0.20		0	+0.15	−0.15
7	0	−0.25	+0.25	17‡	+0.30	+0.45	−0.15
	+0.10	−0.15	+0.25		+0.20	+0.50	−0.30
8‡	−0.05	0	−0.05	18	−0.35	−0.50	+0.15
	−0.10	+0.05	−0.15		−0.40	−0.35	−0.05
9	−0.25	−0.15	−0.10	19‡	+0.10	−0.10	+0.20
	−0.15	−0.05	−0.10		+0.10	−0.10	+0.20
10	0	−0.10	+0.10	20	+0.25	+0.40	−0.15
	+0.15	−0.15	+0.30		+0.20	+0.55	−0.35
For all subjects							
First examination, average					+0.03	+0.03	0.00
Second examination, average					+0.01	+0.05	−0.04
Both examinations, average					+0.02	+0.04	−0.02
Mean variation (of mean for one subject)					0.15	0.18	
Probable error (of general mean)					0.02	0.02	
For subjects without glasses, both examinations, average					+0.03	+0.08	−0.05
For subjects with glasses, both examinations, average					+0.03	+0.01	+0.02

* These data were obtained with cylindric trial lenses.
† Lenticular astigmatism was known to exist in the right eye.
‡ Glasses were not worn.

Although it is evident from table 2 that the "average" correction prescribed from the usual tests and that indicated by dynamic sensitometric examination are in virtual agreement, it is rather probable that this agreement is empiric. While the refraction found by sensitometric examination is based on the actual attainment of maximal visibility, the usual diagnoses are based on technics which have been modified to yield satisfactory prescriptions. Some of these modifications are due to (1) technics which may permit the functioning of relative accommodation;

8. Sheard, C.: Dynamic Skiametry and Methods of Testing Accommodation and Convergence of the Eyes, Chicago, Cleveland Press, 1920, p. 108.

(2) the adding of as much plus power (in certain cases) as is possible without materially reducing visual acuity, and (3) the practice of "fogging" vision with convex lenses until some arbitrary degree of visual acuity is obtained. If the usual technics did not result in reasonably satisfactory prescriptions for the majority of subjects, they could be modified so as to achieve this objective, since the procedures are flexible. In fact, it is more than an assumption that such modifications have been made as a result of many years of clinical experience.

Since the data of table 2 were obtained with cylindric lenses, it might be argued that (1) these sensitometric indications of emmetropia at the near point resulted from accommodation to the convergence target and (2) that the individual departures from emmetropia are merely indicative of uncorrected astigmatism. Thus the fact that symmetric and peaked relations were obtained between visibility and refraction with cylindric lenses is not proof that accommodation to the convergence target was avoided, since the visibility of the latter was not

TABLE 3.—*Refraction Indicated by Successive Examinations at the Near Point with Cylindric and Spherical Trial Lenses, Respectively* *

Time of Day	Cylindric Lenses (O. D.)				Spherical Lenses (O. U.)					
	Monday	Tuesday	Wednesday	Average	Thursday	Friday	Monday	Tuesday	Wednesday	Average
9 a.m.	—0.25	—0.10	0.00	—0.12	—0.15	—0.10	—0.05	—0.15	—0.15	—0.12
5 p.m.	—0.15	—0.15	—0.10	—0.13	—0.10	—0.15	—0.05	—0.10	—0.10	—0.10

* The subject has never worn glasses.

appreciably altered by the cylindric lenses. As a check test, all of the subjects were examined with spherical trial lenses instead of cylindric lenses. In addition, a number of subjects were examined with spherical lenses of equal powers before both eyes. In all instances reasonably symmetric and sharply peaked relations between visibility and refraction were obtained. Obviously, if the accommodation were adequately stimulated by the convergence target or the trial lenses, a plateau rather than a peak in visibility would result with spherical trial lenses varying from + 1.0 to a — 1.0 diopter. Since no semblance of a plateau was obtained in any case, it may be assumed that accommodation was inhibited. In general, cylindric lenses are preferred for clinical use, since the optical characteristics of the convergence target are not altered by the trial lenses. This minimizes the probability of disturbing the habitual dominancy. In addition, the use of cylindric lenses eliminates adjustments for interpupillary distance.

The reproducibility of the dynamic measurements is emphasized in detail by the data presented in table 3. These data include the results of six consecutive examinations with cylindric lenses (right eye) and ten consecutive examinations with spherical lenses (each eye) at a

fixation distance of 16 inches. Subject 8 was selected for this investigation, since both eyes were emmetropic or nearly so. It will be noted from table 3 that the refraction at the near point is substantially the same at all examinations, thus indicating that the sensitometric examination may be made either with cylindric or with spherical trial lenses.

The data obtained with spherical lenses before each eye are plotted in figure 6 and are indicated by the solid circles. The data obtained by geometric construction according to the "3 point method" are shown by open circles. It is evident from these graphs that relative accommodation was not exercised to any discernible degree during the course of measurements at the near point. In other words, there is no indication of plateau in the visibility-refraction relation in any of the ten consecutive series of measurements. These data are typical in this respect of those obtained in all other cases by the dynamic sensitometric method and indicate the precision of such measurements.

In appraising the effectiveness of the ophthalmic corrections prescribed by the usual technics, it is of particular interest to consider persons with emmetropia who do not use glasses. The physiologic states of the eyes of such persons are those which have evolved from natural causes and thus do not involve the judgment of the refractionist in effecting compromises. It will be noted from table 2 that the average sensitometric finding at the near point for persons who have never worn glasses indicates emmetropia. In brief, the average data obtained by the sensitometric method are in substantial agreement with those derived from analyses of a series of usual tests.

The data of table 2 also show that the same refraction is obtained by dynamic sensitometric examination for both eyes when the algebraic averages are considered. A similar conclusion also follows from an analysis of the data obtained by static sensitometric examination (table 5). If it is assumed that the average monocular corrections for this group are proper, it follows that the sensitometric procedures do not introduce biases which might conceivably arise from such factors as ocular dominancy or unbalanced visual stimuli for convergence.

An Experimental Appraisal of Ocular Comfort.—The assumption that the corrections worn by our group of subjects and prescribed by modern technics are reasonably accurate on the whole is in harmony with our data pertaining to ocular comfort, as the latter is revealed by the frequency of blinking.[9] The significance of this criterion of ocular strain or effort is suggested by the statement of Ponder and Kennedy[10] that "the rate of blinking is closely related to the mental tension of the

9. Luckiesh, M., and Moss, F. K.: The Eyelid Reflex as a Criterion of Ocular Fatigue, J. Exper. Psychol. **20**:589, 1937.

10. Ponder, E., and Kennedy, W. P.: On the Act of Blinking, Quart. J. Exper. Physiol. **18**:89, 1927.

subject at the time and that in all probability the movements constitute a kind of relief mechanism whereby nervous energy otherwise unutilized passes into a highly facilitated path." Furthermore, Blount [11] concluded "that one of the reasons for blinking is to allow alteration to take place in the tension of the ocular muscles and thus eliminate early fatigue." These considerations are strongly supported by the results which we have obtained in applying the criterion of involuntary blinking as a measure of ease of seeing in various major researches involving diverse visual situations.

In a recent research [12] the criterion of the frequency of involuntary blinking was applied as an indication of the relative ocular comfort in reading afforded by different ophthalmic corrections. For example, the data of table 4 show the average frequency of blinking for a group of 30 subjects (including many of the subjects listed in table 2) while wearing (1) + 0.50 diopter spheres, (2) plano lenses and (3) — 0.50 diopter spheres in addition to their usual corrections, if any.

TABLE 4.—*Number of Blinks Occurring During Five Minute Periods of Reading with Corrections of + 0.50 Diopter, Plano Lenses and — 0.50 Diopter, Respectively in Addition to the Corrections Usually Worn*

	+0.50 D.	Plano Lens	—0.50 D.
Averages for all subjects	37.1	25.9	36.1
Probable error*	2.8	2.0	2.9
Averages for 17 subjects with corrections	36.2	27.3	38.5
Probable error*	4.0	3.1	4.8
Averages for 13 subjects without corrections	38.4	24.1	33.0
Probable error*	3.9	2.5	3.4

* The probable errors include the systematic differences in blinking among subjects.

Considering the reactions of these subjects as a group, it will be noted that the average rate of blinking is increased by the addition of either convex or concave spheres. This is an indication of the accuracy of the corrections worn by the subjects in the present investigations. This conclusion is supported by the agreement between the results obtained (1) by the usual methods of refraction, (2) by dynamic sensitometry and (3) by the actual appraisal of ocular comfort at the near point. A correlation of these results reveals that maximal visibility and ease of seeing are obtained concomitantly. Furthermore, the data of table 4 indicate that the exercise of relative accommodation (either positive or negative) during reading involves an expenditure of effort. Thus it is not justifiable to assume that the mechanisms of relative accommodation may be employed, without penalty, in compensating for any error in diagnoses and prescription.

11. Blount, W. P.: Studies of the Movements of the Eyelids of Animals: Blinking, Quart. J. Exper. Physiol. **18**:111, 1927.

12. Luckiesh, M., and Moss, F. K.: Frequency of Blinking as a Clinical Criterion of Ease of Seeing, Am. J. Ophth. **22**:616, 1939.

STATIC SENSITOMETRIC EXAMINATION

The principles and procedures for determining the refractive states of the eyes at the far point are precisely the same as those of dynamic sensitometric examination. Obviously, this characteristic is a desirable one for revealing muscular phenomena associated with these fixation distances, even though it may not be of great importance in the direct prescription of ophthalmic corrections. The data obtained by static sensitometric examination with spherical lenses are presented in table 5 and represent the average of two separate examinations in each case. The corresponding data obtained by dynamic sensitometric examination are also presented to facilitate comparison.

Data Obtained by Static Sensitometric Examination.—A unique characteristic of the static sensitometric method is that more minus or less plus power has been invariably obtained by this method than by the usual methods of refraction for adult nonpresbyopic subjects. Our conclusion is based on the data obtained on somewhat more than 100 subjects who wore glasses as well as those who had never worn them. In general, these data indicate that in position of "rest" and when the accommodation is not stimulated the image of a distant object is brought to a focus at a point anterior to the retina.

It will be noted from table 5 that the average differential between the static refractions obtained by the sensitometric method and that obtained by the usual methods is of the order of 0.75 diopter with a corresponding probable error of 0.05 diopter. Furthermore, an average dioptric differential of this order was obtained (1) for subjects wearing their usual corrections, (2) for subjects who had never worn glasses and (3) for both the right and the left eye of all subjects. It is probably significant that this value is in agreement both in magnitude and in algebraic sign with the refractive differentials obtained by retinoscopic examination under static and dynamic conditions. However, this finding does not indicate that the so-called emmetropic subject is actually handicapped in distant vision by an actual refractive error of 0.75 diopter, since it is a reasonable assumption that at least a part of the sensitometrically indicated differential (revealed when accommodation is avoided) is eliminated by negative relative accommodation.

Although the average differentials in refraction indicated by the sensitometric method and by the usual methods are almost identical for the two groups of subjects, it will be noted that the differentials among individual subjects are rather large. Even within this small group of subjects the latter vary from slightly over 0.125 diopter to about 1.50 diopters for the extreme values notwithstanding the fact that these subjects, with their corrections, would be considered as emmetropic, or nearly so. Thus it appears to be an unequivocal fact that these subjects

are far from alike as visual reactors, notwithstanding their approximate similarity with respect to visual acuity at the far point. Although the static sensitometric data contribute to a better understanding of the functioning of the accommodative mechanism of the subject, it is recognized that these data are not appropriate for the direct prescription of ophthalmic corrections. Nevertheless, if a correction factor of 0.75 diopter is applied to the static refraction (as is customary in dynamic retinoscopic examination and as is empirically indicated in

TABLE 5.—*Individual and Average Differentials in Refraction Under Static and Under Dynamic Conditions, as Determined by Two Successive Examinations*

	Static Conditions			Dynamic Conditions			Static Minus Dynamic Values		
Subject	O. D.	O. S.	Differential	O. D.	O. S.	Differential	O. D.	O. S.	Differential
1	−0.82	−0.62	−0.20	−0.40	+0.08	−0.48	0.42	0.70	−0.28
2	−0.30	−0.45	+0.15	+0.12	+0.20	−0.08	0.42	0.65	−0.23
3*	−0.52	−0.48	−0.04	+0.02	+0.02	0	0.54	0.50	+0.04
4	−0.80	−1.00	+0.20	+0.30	+0.10	+0.20	1.10	1.10	0
5	−0.15	−0.45	+0.30	+0.32	+0.08	+0.24	0.47	0.53	−0.06
6*	−0.40	−0.45	+0.05	−0.12	−0.02	−0.10	0.28	0.43	−0.15
7	−0.75	−0.75	0	+0.05	−0.20	+0.25	0.80	0.55	+0.25
8*	−0.95	−0.98	+0.03	−0.06	+0.02	−0.10	0.87	1.00	−0.13
9	−0.75	−0.68	−0.07	−0.20	−0.10	−0.10	0.55	0.58	−0.03
10	−1.20	−1.50	+0.30	+0.08	−0.12	+0.20	1.28	1.38	−0.10
11*	−1.02	−1.02	0	0	−0.12	+0.12	1.02	0.90	+0.12
12	−0.72	−0.80	+0.08	0	−0.02	+0.02	0.72	0.78	−0.06
13*	−0.65	−0.62	−0.03	+0.05	−0.12	+0.17	0.70	0.50	+0.20
14*	−0.95	−0.38	−0.57	−0.02	+0.48	−0.50	0.93	0.86	+0.07
15	−0.65	−0.48	−0.17	+0.15	−0.08	+0.23	0.80	0.40	+0.40
16	−0.70	−0.62	−0.12	+0.02	+0.18	−0.16	0.72	0.80	−0.08
17*	−0.55	−0.08	−0.47	+0.25	+0.48	−0.23	0.80	0.56	+0.24
18†	−1.65	−1.82	+0.17	−0.38	−0.42	+0.04	1.27	1.40	−0.13
19*	−1.05	−0.90	−0.15	+0.10	−0.10	+0.20	1.15	0.80	+0.35
20	−0.55	−0.52	−0.03	+0.22	+0.48	−0.26	0.77	1.00	−0.23
Average	−0.76	−0.73	−0.03	+0.02	+0.04	−0.02	0.78	0.77	+0.01
M. V.	0.24	0.29	0.14	0.15	0.18	0.19	0.22	0.22	0.15
P. E.	0.05	0.06	0.03	0.02	0.02	0.03	0.04	0.04	0.03
				For Subjects Without Corrections					
Average	−0.76	−0.61	−0.15	+0.03	+0.08	−0.05	0.78	0.69	+0.09
				For Subjects With Glasses					
Average	−0.75	−0.81	+0.06	+0.02	+0.01	+0.01	0.78	0.82	−0.04

* Corrections were not worn.
† The subject did not wear sufficient correction.

static sensitometric examination), it will be noted from table 5 that the average data obtained under static and under dynamic conditions are in exact agreement.

In the absence of the sensitometric fixation target and with only a vaguely defined area of brightness for convergence at distance, the sensitometric method indicates that the so-called normal eye is myopic to the extent of 1 diopter. This datum was derived from the average results of two independent researchers: (1) for our group of 20 subjects who are assumed to be free from uncorrected refractive errors and (2) for a group of 25 subjects whose actual uncorrected refractive

errors were measured, respectively, by the sensitometry method and by the actual subjective methods. In both investigations, the differentials in refraction obtained by the two methods were in close agreement. These investigations indicate that the presence of an adequate stimulus for convergence at infinity as compared with the absence of such a stimulus results in a reduction of the average static differential from — 1.00 to — 0.75 diopter. This reduction is attributed to the relaxation of accommodation [13] induced by the stimulus to convergence at infinity.

A Lead of Accommodation.—Since both the static and the dynamic sensitometric refraction are obtained by identical technics, it is evident that the refractive differential is due largely to myopia at the far point, which is revealed when relative accommodation is inhibited by sensitometric means. However, it is emphasized that the distant vision of the "average" subject is not blurred to the extent of this differential (0.75 diopter) since all or a part of this refractive differential may be eliminated by negative relative accommodation. The fact that distant vision is sometimes improved by the addition of minus power to a so-called normal eye indicates that the lead of accommodation is not always fully compensated by negative relative accommodation.

The present discussion of the indicated lead of accommodation at the far point is primarily concerned with the existence of this phenomenon rather than with its causation. In any event, if all stimuli for accommodation are avoided while an adequate stimulus for convergence remains, it appears that the normal adult nonpresbyopic eye is myopic at distance and emmetropic at the near point. It will also be noted from table 5 that the individual subjects vary widely in the indicated lead of accommodation. Thus pseudomyopia might be described as a condition involving a lead of accommodation in excess of that which is counteractable by negative relative accommodation. These are the characteristics which might be expected on teleologic grounds. For example, after discounting pathologic changes, there remains no indication of adaptation to the increased prevalence and importance of near vision unless such adaptation has taken the form of an increased capacity for functional adaptation—a form which would in no way work to the disadvantage of the subject whose visual tasks remain principally long range. On the assumption that presbyopia is inescapable, the best imaginable compromise would give emmetropia at infinity during adolescence and emmetropia at arm's length in middle age, with distant vision still attainable by the exercise of negative relative accommodation. This is almost precisely the average condition found by the sensitometric method as we have defined and developed it.

13. Cogan, D. G.: Accommodation and the Autonomic Nervous System, Arch. Ophth. **18**:739 (Nov.) 1937.

PRIMARY TUMORS OF THE OPTIC NERVE (A PHENOMENON OF RECKLINGHAUSEN'S DISEASE)

A CLINICAL AND PATHOLOGIC STUDY WITH A REPORT OF FIVE CASES AND A REVIEW OF THE LITERATURE

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(Concluded from page 821)

GENERAL COMMENT

Nature of Gliomas as Revealed by This Study.—It is evident from a comparison of sections of the tumors removed from patients in cases 1, 2 and 3 (figs. 14, 23 and 56) that they are essentially the same process, though careful study reveals considerable variation, especially in that part of the tumor which involves the sheath.

When viewed as a group, certain histologic details stand out which suggest five different stages in the evolution of these growths.

At stage 1 there is a generalized hyperplasia of the neuroglia within the nerve stem, with early fiber formation by fibrous astrocytes. The glial cells, both astrocytes and oligodendrocytes, have started to proliferate in an abnormal manner from some unknown cause. The first operative specimen in case 3 illustrates this stage (figs. 39, 40 and 41). The cases reported by Bailey and Herrmann (cited on page 984) and Aegerter and Smith (cited on page 1000) apparently belong in this group. Bailey and Herrmann remarked that "the glial scar was composed of piloid astrocytes." Aegerter and Smith referred to the histologic changes in the optic nerve in their case as a "semi-neoplastic glial proliferation" or "astrocytosis." This term is descriptive for this early stage, though oligoastrocytosis is more so.

Since this stage is evidently the beginning of a true gliomatous proliferation, however, which later takes on more definite neoplastic characteristics, both terms are open to criticism on purely pathologic grounds. Subsequent stages of these growths reveal that a more profound biologic change than simple hyperplasia has taken place. The reaction is neoplastic and malignant, even though of low degree and slow growth. The terms gliomatosis, astrocytosis, etc., should therefore be limited and their use employed merely as descriptive terms for the earliest stage in the development of the new growth.

Stage 2 shows further progress of the growth, as illustrated in the autopsy specimen in case 3 (figs. 1, 51, 52, 53, 58 and 59). Glial proliferation has continued, with the extension of the growth through the pial sheath. Here the arachnoid has likewise become much thickened from a tumor-like growth, due to hyperplasia of the arachnoid cells (figs. 1, 58, 59, 60 and 61). This is distinctly a separate proliferative reaction and not a part of the gliomatous tumor in the nerve stem, though it is sequent to and no doubt dependent on it. It shows none of the staining reactions or other characteristics of the glial tissue, as previously pointed out.

Stage 3 is illustrated by the histologic picture of the tumor in case 2, which in these sections reveals a further step in the growth of the tumor (fig. 21). The glial tumor in the intervaginal space has extended farther out in the sheath, where it has penetrated and invaded the tumor mass in the arachnoid sheath. These tissues become so intermingled that it is difficult to find the normal landmarks in some sections. Study of many sections, however, shows that the growth in the arachnoid sheath has been invaded and either partly destroyed or so compressed that in places it is seen as a thin layer of cells on the outer surface of the gliomatous tumor (fig. 32).

When a tumor has reached this stage of development, if interpretation of its nature is attempted solely from the histologic structure it is manifestly impossible to do more than speculate as to its mode of origin. Glial cells and fibers and arachnoid cells are intermingled in places, and the structure is complex.

Oberling and Nordmann have presented drawings of tumors in this stage (fig. 33); they claimed that the gliomatous growth, far out in the sheath, has arisen from the arachnoid cells, which they call "meningioblasts." They considered these cells of neuroectodermal origin and therefore capable of producing fibers like glial cells. Stage 2, as previously described, clearly shows that the growth in the arachnoid sheath is of a different nature before glial invasion from the nerve stem has taken place. Since the cells bear no resemblance to neuroglia, do not produce fibers and do not take the characteristic stain of glial tissue, it would seem that Oberling and Nordmann's theory is not tenable.

Stage 4 is illustrated in the sections of the tumor in case 1 (fig. 12). The gliomatous growth has destroyed most of the landmarks of the sheath, including the growth in the arachnoid sheath, and only a small remnant of these proliferated cells is seen at the anterior end of the intervaginal space, where the tumor of the nerve stem was less advanced. Even the dura was invaded and partly destroyed by the growth.

Stage 5 (figs. 75 and 76) represents another and more advanced type of these growths. All landmarks within the nerve stem, as well as those of the sheath, are completely obliterated, and the tumor may

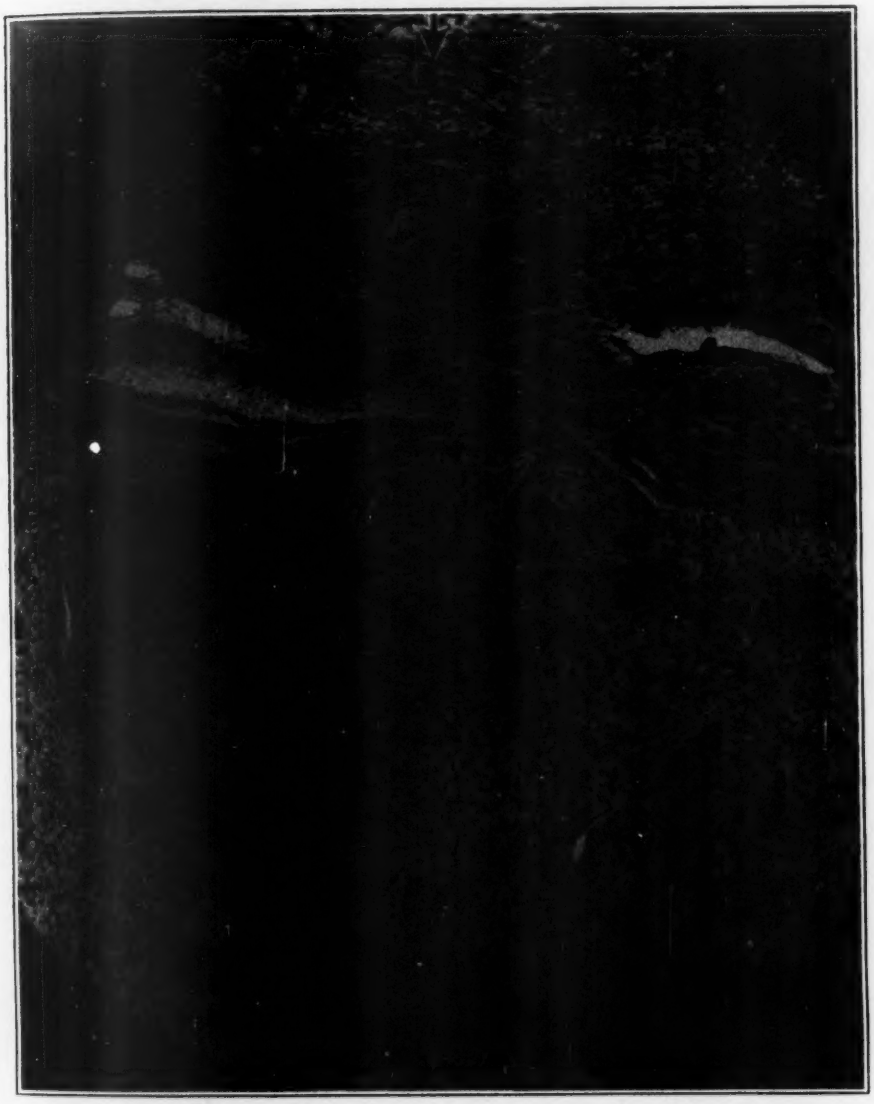

Fig. 75.—Glioma of the optic nerve (advanced, stage 5). Note that the septal partitions are completely obliterated, as well as the sheaths of the nerve. The cells are closely packed and resemble sarcoma. Special stains from this tumor, however, revealed that the cells were chiefly astrocytes. The upper third of the illustration shows the tumor of the sheath. The lower two-thirds shows the tumor of the nerve stem proper. (This specimen was furnished by Dr. W. L. Benedict and is presented with his permission.)

show some characteristics of sarcoma. The cells are spindle shaped and closely packed together. No doubt many of the growths at this stage have been regarded as sarcomas, which they closely resemble. Some of these tumors have been reported as "gliosarcomas."[6] Differ-

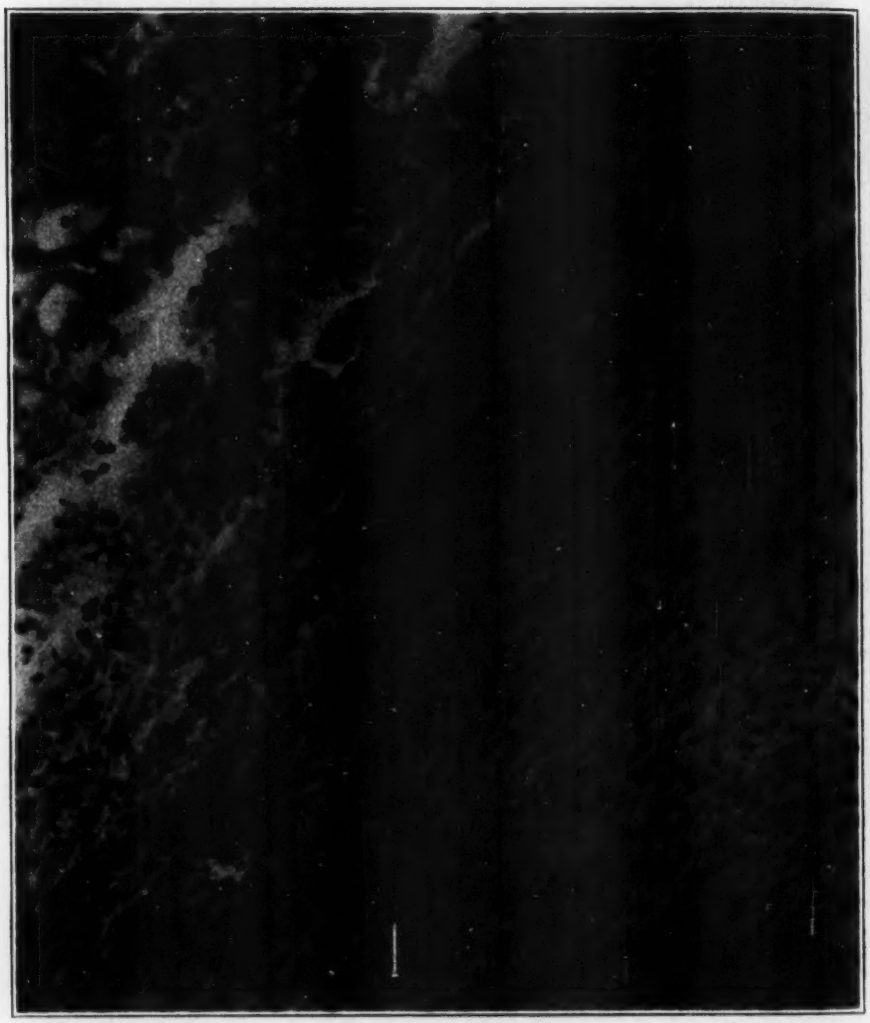

Fig. 76.—Longitudinal section of the glioma in figure 75. This stage resembles sarcoma, with which it frequently is confused.

6. I have recently studied sections from a tumor in Dr. W. L. Benedict's collection which show these characteristics. The tumor was diagnosed as "glioneurosarcoma" (figs. 75 and 76). He gave me a piece of the original specimen, which I sectioned and stained. Masson's trichrome stain, phosphotungstic acid stain and silver stains brought out the typical cellular changes which were found in the tumors which I have described.

ential stains of sections of a tumor of this nature revealed cellular details similar to those in case 2, with marked fiber formation. Large neoplastic astrocytes were found throughout the main body of the tumor (figs. 77, 78, 79 and 80).

Fig. 77.—Section from the main body of a tumor of the optic nerve from an area adjacent to that shown in figure 76. Note the large neoplastic astrocyte and several smaller astrocytes. Oligodendrocytes are also shown (left side).

Verhoeff described three types of tissue in the tumors of the optic nerve which he studied. He divided them into: (1) finely reticulated, (2) coarsely reticulated and (3) spindle cell or coarsely fibrillated. In his detailed descriptions, however, he stated that these types are frequently intermingled in the same tumor, variations depending on the place in which the section was cut.

The myxomatous appearance of some of these tumors is indicated by the frequency with which writers attach the term "myxo" in describing the growth. This has not been a prominent feature of any of the tumors I have studied, though in case 1 the tumor tissue in the nerve sheath

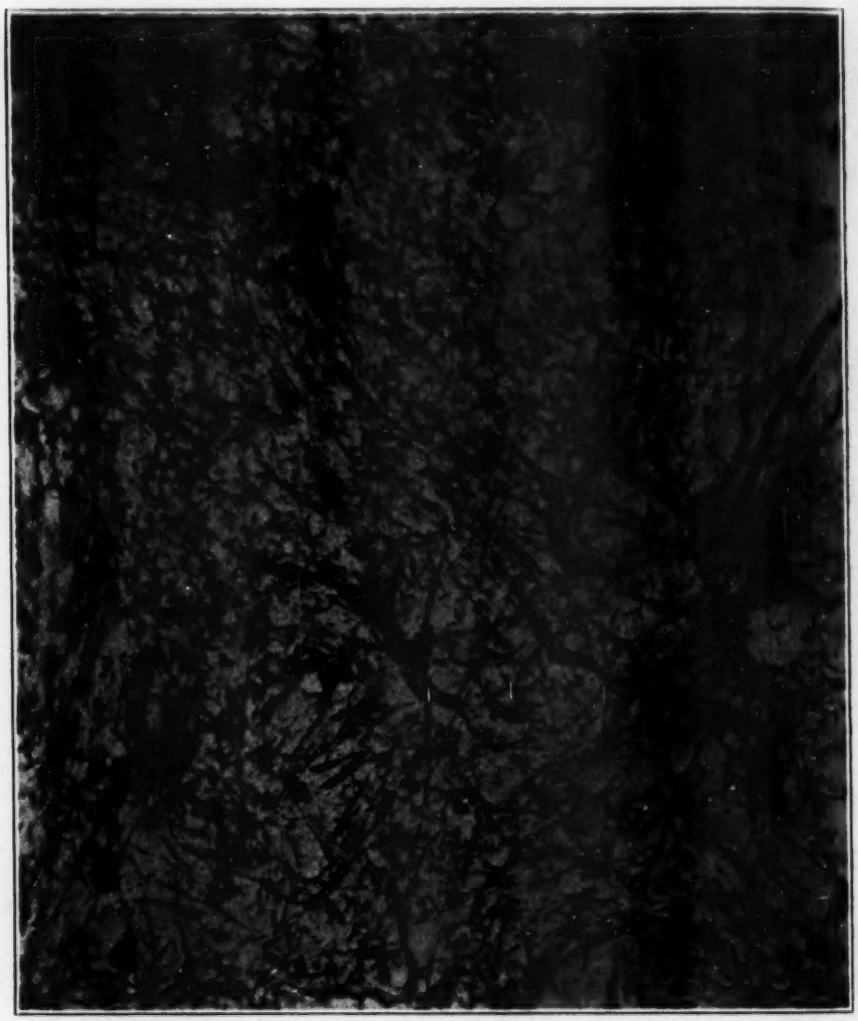

Fig. 78.—Transverse section through a tumor of the nerve stem from the area adjacent to that shown in figure 75 (Weil-Davenport ammoniacal silver technic; × 500). Note the much enlarged neoplastic astrocytes and few oligodendrocytes. (The gross specimen was furnished by Dr. W. L. Benedict. It was sectioned and stained in the pathologic laboratory of the ophthalmic department of the Wisconsin General Hospital.)

was loosely arranged and riddled with vacuoles and small spaces. No mucoid material was found in these spaces.

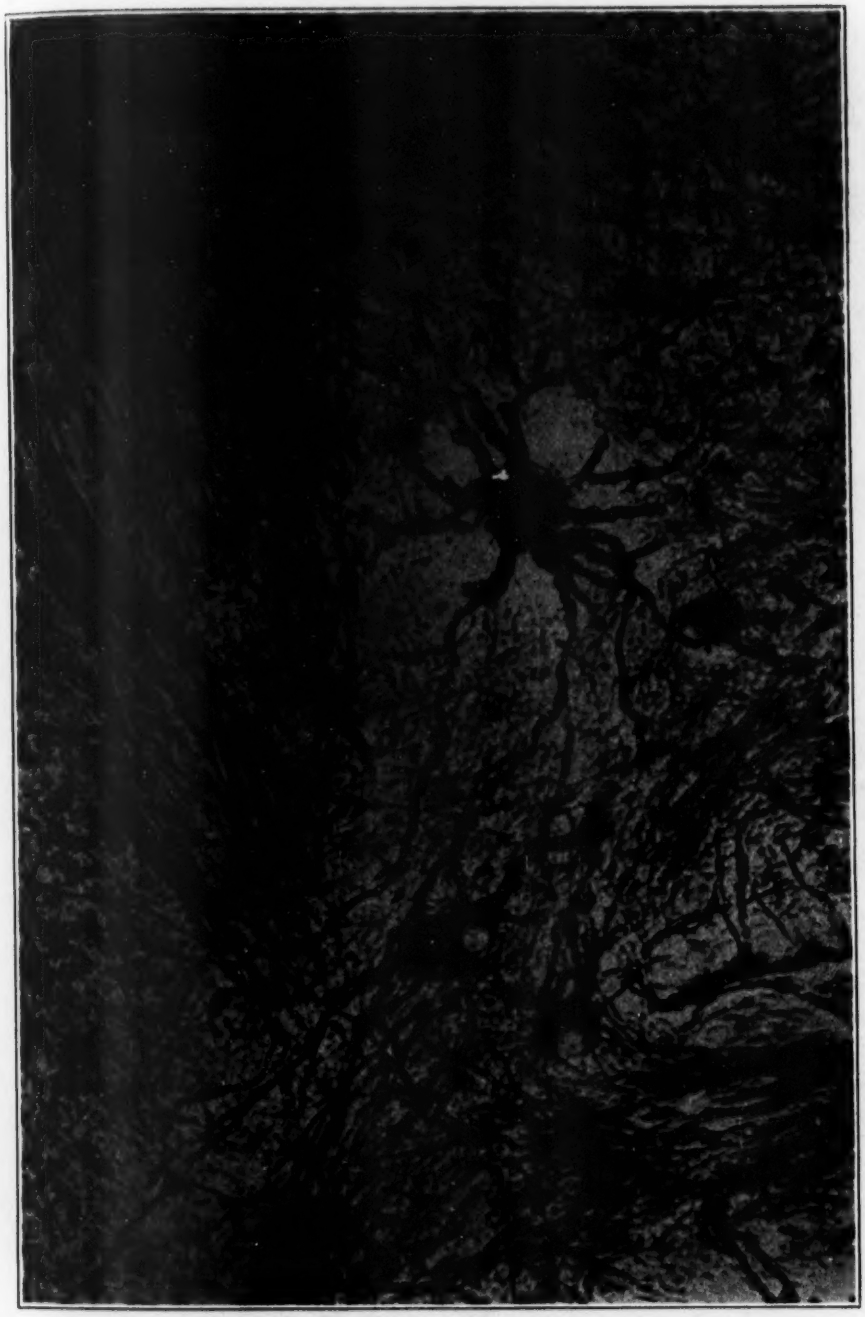

Fig. 79.—Huge swollen neoplastic astrocyte and three oligodendrocytes (one large cell above, with short processes; two smaller cells below) from the tumor (shown in figure 78) of the nerve stem (Weil-Davenport stain; × 800). Note the exceedingly long processes which extend out from the body of the astrocyte. These resemble Nissl "plump cells."

Fig. 80.—Swollen neoplastic astrocyte, type cell of tumor; × 1,500.

Verhoeff has discussed the proliferation of arachnoid cells which is frequently associated with gliomas and has suggested that its origin is purely mechanical, resulting from a distention of the subdural space and consequent strain on the arachnoid trabeculae. He admitted, however, that some stimulating influence from the glioma may be the underlying cause, though he expressed doubts concerning this, since the tumor does not tend to stimulate other connective tissue even when in direct contact with it. It is true, as shown in sections from these tumors, that connective tissue of the septums is not "stimulated" to growth, though there is at times some thickening of the pia. The cells of the arachnoid, however, are a special type of mesothelial cell and seem to react in a manner different from ordinary fibroblasts. Whether they react from strain, as suggested, or from direct stimulation of the glial proliferation which has invaded the sheath or from some independent growth stimulus is impossible to state in the present state of knowledge.

Von Hippel, however, was so impressed by this feature of glial tumors that he suggested the term "fibrogliomatosis," thereby definitely indicating that fibrous elements participate in the growths.

Since the gliomatous proliferation of the nerve stem precedes the growth in the arachnoid sheath, as shown in case 3, it would appear that proliferation of the mesothelial cells of the sheath is a simple process of reaction in the effort to wall off and surround the new growth as it invades the subarachnoid spaces.

The origin of the tumors is uncertain. Case 3 (first operative specimen) indicates that they begin with a generalized abnormal proliferation of adult neuroglia of the nerve stem. In the less affected areas the cells bear a striking resemblance to normal neuroglial cells, that is, to astrocytes and oligodendrocytes. While some authors refer to these areas as preneoplastic gliosis and Hudson designated the full blown tumor as a "degenerative gliomatosis," they are in reality true neoplasms, as is evident if one follows the progress of the growth, as outlined previously. The cells show pleomorphism, hyperchromatism and unnatural arrangement, and they finally definitely invade surrounding structures. Therefore, I agree with Verhoeff that they should be classified as gliomas and not as "degenerative gliomatosis," as suggested by Hudson and others.

The extremely slow rate of growth and the relatively benign nature of these tumors, however, suggest that they do not arise from cells of embryonic type. Since many of these tumors seem to be definitely associated with generalized neurofibromatosis, they no doubt arise from the same cause.

Bilateral involvement of the optic nerves has been frequently reported. Strawbridge, H. Knapp, Goldzieher, Adamuk, Willemer and others have reported cases in which the second eye became blind. Early glial changes were evidently present in the nerve of the left eye in my case 3, as indicated by the advancing atrophy of the nerve head.[7]

Emanuel early directed attention to the formation of multiple tumors in the optic nerve and cited 10 cases in which this was reported. No doubt cases of multiple involvement of the nerve may be more common than has been supposed, since early study is often impossible. Further, many of the tumors which have been reported have not been serially sectioned throughout the entire length of the nerve. The intracranial section of the right nerve in case 3 indicated the beginning of a new and separate focus from the main tumor, since it was fairly sharply separated. The entire nerve, however, was more or less affected, so this area may have been a more active focus. Furthermore, many of the tumors have been removed at such an advanced stage of growth that a large part of the nerve has become involved through gradual enlargement of the tumor.

Verhoeff suggested that in his case 1 the actively proliferating neuroglia of the tumor may have produced hyperplasia in the adjacent areas of relatively normal nerve as well as in the retina. It seems to me just as reasonable to assume that different areas within the nerve are gradually affected by the same underlying cause, some at one time and others at another. The theory of some "stimulating factor" as a general unknown causative agent appears plausible, but it seems unnecessary to invoke this as an explanation of the local progression of the growth. The growth would naturally spread from a gradual increase in size by contiguity, or it may well be the development and merging of separate foci within the nerve. As has been shown, the chiasm also is not infrequently affected as are other areas within the brain. These areas obviously do not always arise through spread of the growth from one to the other but probably develop in the same manner as described—from independent or multiple areas which take on abnormal growth.

Since many of the tumors, particularly the gliomas, are probably congenital in origin, some authors suggest a congenital rest or "anlage" due to abnormality in embryonic development. If the disease is indeed but a part of the Recklinghausen syndrome, it seems unlikely that the tumors arise in this manner. Ida Mann expressed the belief that the general lesions of Recklinghausen's disease are not related to any particular embryonic stage of development and that they are pure aberrations of growth.

7. The patient in case 2, readmitted to the ward since the completion of this paper, shows evidence of an early tumor in the right optic nerve and possibly in the brain. There is still no evidence of local recurrence in the left orbit.

Martin and Cushing have directed attention to the fact that gliomas of the optic nerve and chiasm differ in some ways from some of the gliomas of the brain, but they suggested that cerebral gliomas which follow a particularly benign and favorable course may have been of this nature. More malignant cerebral gliomas evidently arise from cells of embryonic type.

A further reference to the specific types of glial cells which have been reported in tumors of the optic nerve will be found in another section of the paper.

The presence of "cytoid bodies" in these tumors has been discussed by Verhoeff. He has given somewhat varying descriptions of the bodies in two articles he has published. In one he referred to them as "atypical or giant neuroglia fibrils"; in a later communication he stated that they are found in these tumors as well as in pathologic conditions of the retina, and he described their origin more in detail. He expressed the belief that they arise within the neuroglia syncytium through deposition of a substance derived from disintegrating red blood corpuscles. He stated that they occur only at the site of previous hemorrhages.

Martin and Cushing referred to these bodies as "masses of neuroglia," which they stated are not infrequently found in gliomas elsewhere, although differently termed.

Cone and McMillan discussed the formation of cytoid bodies in the unmyelinated nerve fibers of the nerve head. They described interstitial edema and swelling of nerve fibers in papilledema, followed by degenerative changes and deposition of fine granules in the enlarged and swollen fibril. These enlargements eventually lose their relation to the nerve fibers and at this stage are called "cytoid bodies."

Some of these bodies were present in the tumor in the nerve sheath in 2 of my cases, and a few were noted among the masses of neuroglial fibers of the nerve stem in case 3. No particular study of them was made. They appeared in areas in which neuroglial fibers were particularly coarse and dense.

The study of two different eyes in which the optic nerve was severed is of interest. In case 2 the eye was not removed, so only ophthalmoscopic changes were followed. This showed that the retinal vessels do not always collapse after severance of the nerve, which is explained by anastomosis of the vessels of the ciliary and retinal systems. The absence of typical pigmentary degeneration of the retina indicates that this layer of the retina was also well nourished. Since the ganglion cells must have degenerated, as shown in case 3, this evidently does not influence the retinal pigment layer.

The histologic picture of the enucleated globe in case 3 is somewhat altered, no doubt, by the presence of the neurofibromatosis of the nerves

of the choroid. The pigment epithelium was degenerated, and in places the cells were devoid of pigment, since it had wandered into the inner layers of the retina. In large areas the pigment granules, though somewhat broken up, remained in the cells. The complete degeneration of the ganglion cells and the almost total absence of blood vessels in the retina were noted.

Apparently the ciliary vessels were not seriously damaged in case 2, while in case 3 the amount of damage is uncertain because the replacement of the normal choroidal tissue by neurofibromatosis somewhat alters the picture. Blood vessels were still present throughout the choroidal tumor, but they were reduced in size and number. The globe was evidently well nourished.

Clinical Features.—In addition to the well recognized signs of primary tumors of the optic nerve outlined in the beginning of this paper, the importance of roentgen studies of the optic foramens and the region about the sella turcica should be particularly stressed.

Enlargement of the optic foramen is an important diagnostic sign, as stressed by van der Hoeve, Arnold Knapp and others. It is not always present, since the tumor may be confined to the middle or anterior portion of the nerve, at least for some time. The posterior end of the nerve may eventually become affected, however, so roentgenograms should be made periodically. I have used the method of Goalwin, which has proved satisfactory. The measurement of the exact size of the canal, according to Goalwin, depends on the size of the spot of the x-ray tube, the distance of the spot from the plate and the distance of the optic canal from the plate. The last is naturally variable. From a practical standpoint, it is the difference in the size of the canals of the two sides which is of greatest importance, particularly in the case of suspected unilateral tumor of the optic nerve. Goalwin estimates the average size of the canal as 4.3 by 4.4 mm., with variations from 3.25 to 5.5 mm. These measurements would be approximately 1 mm. larger on the film.

Roentgenograms of the foramens proved helpful in 4 of the cases herein considered. Enlargement was questionable in case 2. In case 3 there was no enlargement at the time of the first examination, but a definite increase in the size of the foramen appeared about two years after the child came under observation. In cases 4 and 5 there was a slight increase in the size of the more affected side.

Roentgen studies of the region of the sella turcica may be helpful in the diagnosis. A necklike shadow resembling a gourd, extending from the body of the sella turcica under the anterior clinoid process, was present in 2 of the cases herein reported. This peculiar deformity anterior to the sella turcica was first noted in this connection by Martin

and Cushing and described in their excellent paper concerning primary gliomas of the chiasm and the optic nerves in their intracranial portion. I consider this a contribution of outstanding importance. Roentgenologists apparently are not generally aware of the significance of this shadow. The films in 6 of Martin and Cushing's cases revealed the defect, though with one exception they were originally reported to be within normal limits. In my cases 1 and 3 the roentgenographic picture in the region of the sella turcica likewise was reported within normal limits until the shadow had grown to considerable size (fig. 45). A rereading of the earlier films revealed the presence of this significant shadow. In case 2 a vague outline of this shadow was seen, but I consider this inconclusive. In case 4 there is only a slight suggestion of the shadow at present, probably because the chiasm was most likely the primary seat of the lesion and the growth in the optic nerve was less advanced. This suggests that an increase in the size of the optic nerve and consequent erosion of the optic canal may be the chief cause of the shadow.

Martin and Cushing are cautious in their comments concerning the importance of this sign, since pear-shaped sellas unassociated with atrophy of the optic nerve have been reported. They cited the short paper by Timme, who reported a similar deformity in 23 of 24 cases of mongolian idiocy. Roentgenograms made in 2 such cases recently studied in the Wisconsin General Hospital did not reveal any abnormality about the sella turcica in 1 of them. In the other case there was a slightly suggestive shadow which in some ways resembled those found in cases of tumors of the optic nerve. It appeared more like a thickened and elongated anterior clinoid process. The progressive nature of the lesion in tumors of the optic nerve is revealed by the gradual increase in the size of this shadow, as shown in the films in case 3.

I have attempted to reproduce this peculiar shadow experimentally on dry skulls by enlarging the optic canal and introducing various opaque substances, such as lead and gum impregnated with barium. The experiments were not absolutely conclusive, but by breaking down the roof of the canal and undermining the anterior clinoid process a shadow resembling it could be obtained.

If the chiasm is involved by the lesion, changes in the visual fields are of great assistance in diagnosis. Often the patients are too young to obtain a satisfactory field of vision, as in the first 3 cases herein reported. In cases 4 and 5, however, the studies were invaluable. The temporal hemianopia was fairly cleancut in one eye in each case, while the fields of the other eye, though less typical, were suggestive of a temporal defect. Cushing stated that defects in the visual fields, though often bitemporal, are apt to be bizarre and that hemianopia with a vertical meridian is rare. In 2 of the cases he recorded, however (9 and 9-a),

sharply cut temporal hemianopia was present on one side; in 1 of these cases the hemianopia of the other side was less typical but suggestive, while in the other there was only a patch of retained vision for moving objects in the upper temporal field.

Martin and Cushing have emphasized the clinical fact that in cases of tumor of the pituitary body unilateral blindness is not uncommon, but central vision of the fellow eye may long remain normal or be only slightly altered. They stated, however, that in cases of glioma of the chiasm vision is markedly diminished in the less affected eye. This is of importance in a differential diagnosis of a gliomatous lesion of the chiasm, and case 5 appears to confirm this. Central acuity remained good in case 4, but changes in the visual fields were typical. If the tumor of the optic nerve is confined to the intraorbital portion of the nerve, this differential point will fail, since the fellow eye is usually unaffected. The change in the visual field of the affected eye in these cases, however, is usually unlike either that seen in cases of tumor of the pituitary body or of glioma of the chiasm, so confusion should not arise.

The extreme youth of most of the patients with glioma should again be stressed, for it indicates that many of the lesions are congenital in origin. They have, however, been reported as late as the sixtieth year.

Marked reduction in visual acuity may precede exophthalmos. It is more likely to occur when the chiasm and the intracranial portion of the nerve are the primary seat of the lesion. This is well illustrated in the histories of cases 4 and 5.

Failure of vision may progress slowly. Cushing directed attention to this fact and remarked that it may be stationary for a considerable period. The vision in 1 of the cases reported by Martin and Cushing remained essentially unchanged after an interval of seven years. In case 5 of my series the reduction in visual acuity evidently began in earliest childhood, since the patient stated that she could not recall a time when she had good vision. She was 27 at the time of admission to the hospital, and some remnant of vision still remained.

Trauma is mentioned in many case histories reported in the literature. While it seems unlikely that trauma produces the tumor, it may contribute to the progress of its growth. It is mentioned with sufficient frequency to warrant some consideration.

Treatment consists of operation, which is almost universally advised except in cases in which the chiasm is involved. It has been satisfactory so far as the local growth is concerned. Recurrence is rare. It has been stated by most authors that local recurrence of the tumor in the orbit never occurs, but Emanuel cited 3 cases in which the growth reappeared (that of Szokalski after a lapse of five years, that of Goldzieher after one year and that of Parisotti and Despagnet after three months). Endotheliomas also recur locally at times.

Case 3 of this series might be placed in this category, but in this instance no attempt was made to remove the entire nerve, since it showed no evidence of tumor on gross inspection. In many instances the intracranial portion of the nerve may be involved, so that the final outcome must remain uncertain. In most of the cases in which autopsy is performed some form of intracranial involvement has been found. This may have developed through direct extension of the growth or, more likely, through the further development of an independent lesion within the brain. Since many of these tumors are unquestionably only a part of a generalized involvement of other neural structures, the ultimate prognosis is extremely grave, at least in those associated with Recklinghausen's disease.

Most authors advise removal of the tumor with preservation of the globe. Herman Knapp was among the first to practice retrobulbar excision of the tumor without removal of the globe. He approached the tumor through the conjunctiva. In his first case the cornea sloughed and the globe was lost. A similar result has been reported by a number of observers. Fuchs, in his text stated: " . . . the ciliary ganglion is usually injured by this procedure with subsequent degeneration of the globe." Many authors advocate the Krönlein procedure, and some approach the tumor through an incision in the brow.

The method employed in cases 2 and 3 was satisfactory from a cosmetic standpoint. The approach is reasonably simple, and, judged by the results in these cases, the nutrition of the eyeball is not seriously affected. I have used this operation on two other occasions for the removal of hemangiomas of the orbit. The tumor can be more effectively exposed if the inferior rectus muscle is detached and later sutured with chromic catgut. Now that it is known that chromic catgut can be buried in the episcleral tissues with impunity, a procedure I have used for more than seven years, there is no reason why this should not be carried out.

Death from meningitis has been reported following removal of the tumor by various procedures (Hudson, 10 per cent).

Dandy, in commenting on the frequency with which intraorbital tumors extend into the cranial cavity, suggested the transfrontal intracranial approach for the removal of the growths. He strongly condemned the conjunctival route, since, according to Hudson's statistics, the incidence of meningitis and death has been so high. Dandy stated: "No operation should be performed through a field which cannot be sterilized and protected." While this statement may be endorsed on general principles, the ophthalmic surgeon must none the less constantly face this hazard.

The operative procedure which I have used, namely, through the skin of the lower lid, offers a greater measure of safety from infection because the field of operation can be sterilized. The anterior orbital approach to the tumor is infinitely more simple and safe than the formidable transfrontal route. Unless there is evidence of chiasmal involvement or definite signs of massive extension of the tumor into the cranium, it would seem that some procedure of this type should be the method of choice.

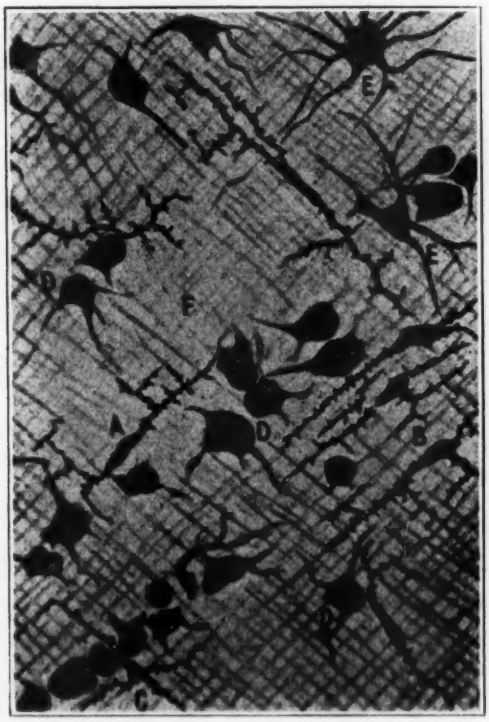

Fig. 81.—Diagrammatic drawing of neuroglial cells in a longitudinal section of the chiasm. *A*, *B* and *C*, microglia (Hortega cells); *D*, oligodendroglia; *E*, an astrocyte (fibrous neuroglia), and *F*, nerve fibers. (From Enriquez, L.: Bol. r. Soc. españ. de hist. nat. **26**:301, 1926.)

Decompression of the nerve by unroofing the optic foramen may be of temporary benefit when the tumor involves the intracanicular and intracranial part of the nerve adjoining the chiasm. Several authors, cited in the bibliography, reported successful results from this procedure. In one case visual improvement has extended over a period of ten years, while in another there has been improvement for a period of two years. This operation was carried out, as noted, in case 5. It should be performed by the neurosurgeon, though the collaboration of the ophthalmologist should be of value, particularly if the orbit is explored.

GLIAL CELLS OF THE NORMAL OPTIC NERVE

Before citing the different types of gliomas which have been reported by authors who have made an especial study of this phase of the glial tumors, a brief reference will be made to the nature of the glial elements of the normal nerve.

The optic nerve, like the olfactory, is not a nerve in the true sense but is in reality a tract, comparable to the intracerebral pathways of the white matter of the brain. There are, however, definite variations, due in part to the subdivision of the tract into bundles, or funiculi, which

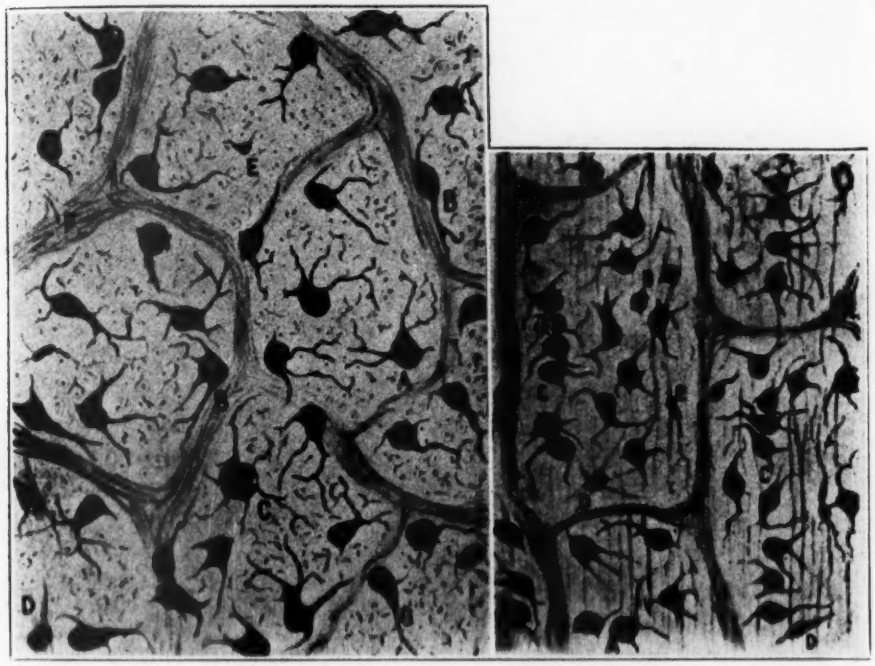

Fig. 82.—Diagrammatic drawings of neuroglial cells of the normal optic nerve and chiasm. On the left, oligodendroglia in a transverse section of the optic nerve. *A* is a typical oligodendroglia; *B*, a gliocyte near a connective tissue septum; *C*, a gliocyte of the spongy type; *D*, fibrous neuroglia; *E*, microglia; *F*, connective tissue septums, and *G*, gliocyte of the comet type.

On the right, oligodendroglia in a longitudinal section of normal optic nerve. *A* is a typical oligodendrocyte; *B*, a small oligodendroglia; *C*, oligodendroglia cells in rows (interfascicular); *D*, fibrous astrocytes; *E*, microglia; *F*, connective tissue septums. (From Enriquez, L.: Bol. r. Soc. españ. de hist. nat. **26**:301, 1926.)

are partly enclosed by the fibrous septal expansions from the pia. The individual nerve fibers of the funiculi are further separated by a definite glial network, the cells of which are similar to those found in the white matter of the brain. These cells are of three types, namely, astrocytes,

oligodendrocytes and microglia (fig. 81). Special metallic impregnation methods, such as Cajal gold chloride and del Río Hortega's silver carbonate methods and others, are essential to bring out the cytologic details of these cells. Studies of the optic nerve by Lopéz Enriquez, Marchesani (fig. 82), and Cone and McMillan have demonstrated their presence in the optic nerve.

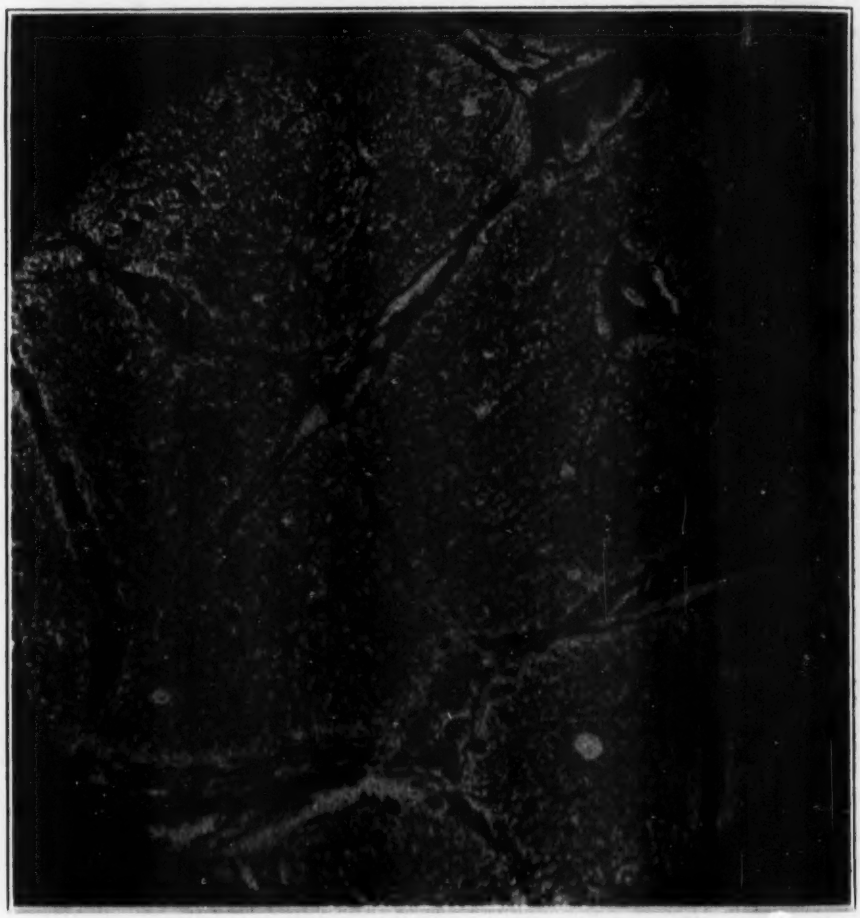

Fig. 83.—Normal optic nerve (Weil-Davenport ammoniacal silver stain; × 300). Note the astrocytes with long processes and a few oligodendrocytes. (This and the remaining photographs show my preparations of normal optic nerve with silver impregnation technic.)

The astrocytes are of the fibrous type and are identical with those in the cerebral tracts (figs. 83, 84, 85 and 86). According to Cone and McMillan, they differ in some ways because of the anatomic variations of the general structure of the nerve. They have a large cell body, from

which cytoplasmic expansions extend in various directions, through which fibers pass. In transverse sections of the nerve these fibers when selectively stained can be seen as a branching network interposed between the nerve fibers, thereby producing a glial framework for their support

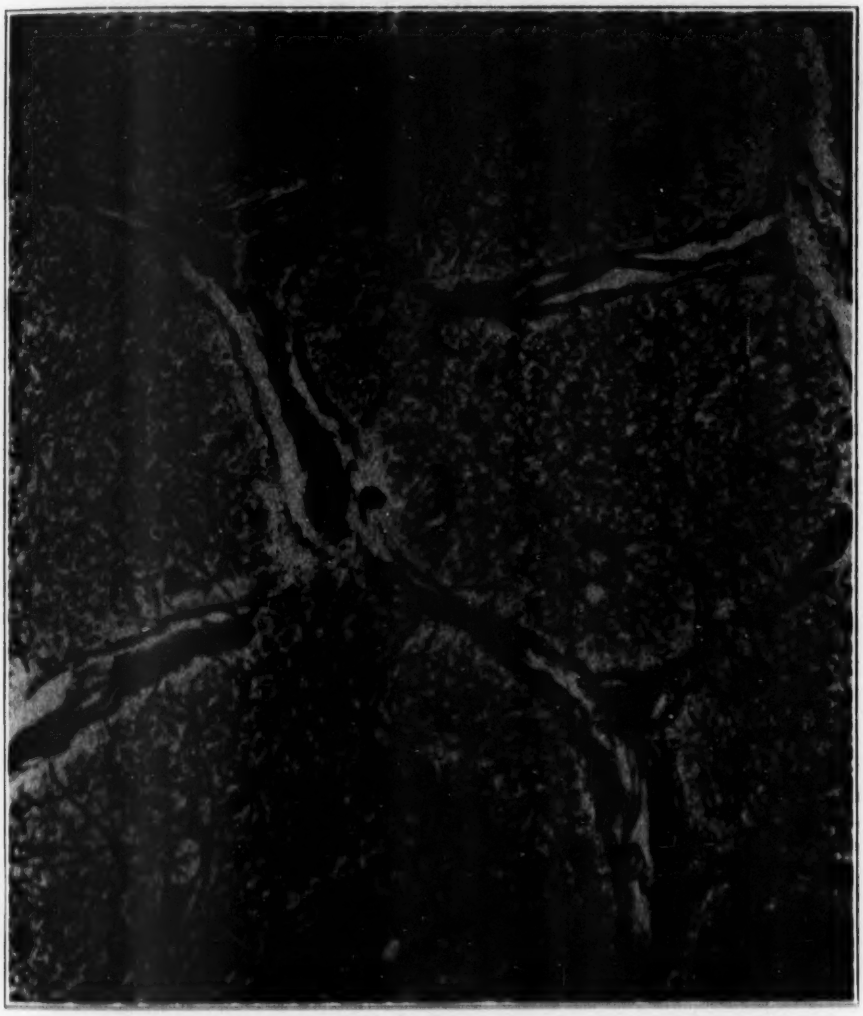

Fig. 84.—Normal optic nerve (× 400). Note the astrocytes with branching processes. The small black points are nerve fibers, surrounded by myelin sheath (white).

(fig. 87). Subpial cytoplasmic expansions as well as subseptal attachments are found as in the brain. These processes, arising from the cells scattered throughout the funiculi, are well shown in figure 88. They can be seen extending in every direction from the cell body, and many

run for a long distance across the funiculus to end on the connective tissue septums. Perivascular attachments are not found, since the blood vessels of the nerve are enclosed within the intraseptal spaces. The fibrous connective tissue septums act as an impassable barrier, no expansions or glial fibers penetrating them in the normal nerve. As has been shown, however, in pathologic conditions, such as tumors, the septums

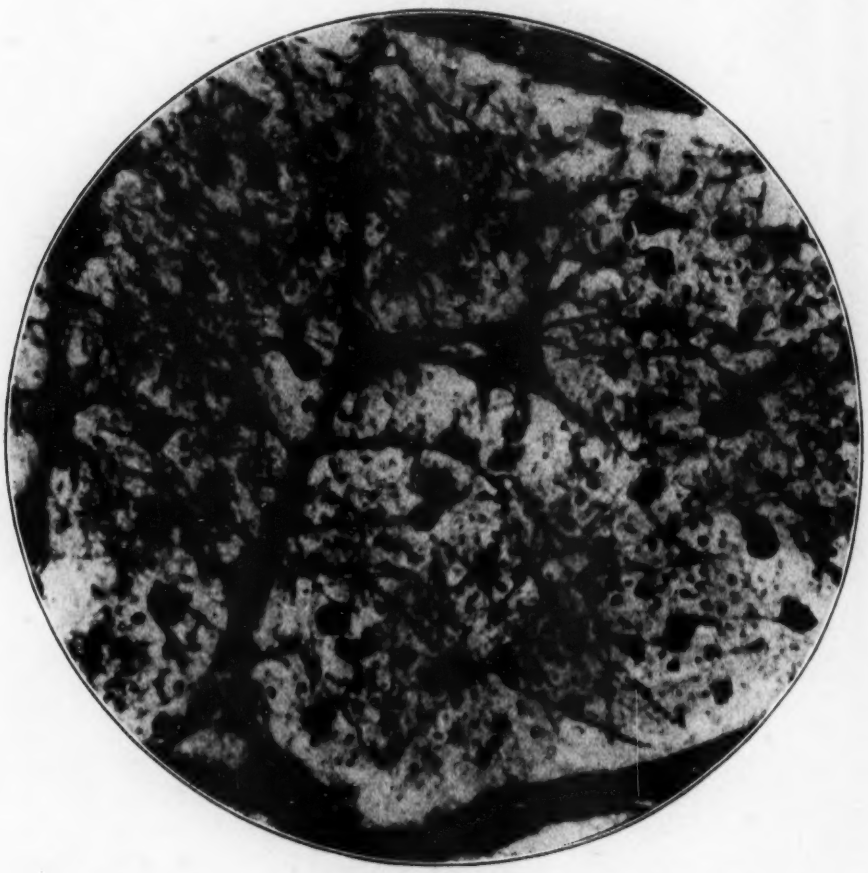

Fig. 85.—Normal optic nerve, transverse section (Weil-Davenport silver stain; × 550). There are several large fibrous astrocytes showing long processes and many oligodendrocytes; some appear as naked nuclei, while others have short processes.

are at times invaded or destroyed through compression. (Figures 89 and 90 show a cross section of a normal nerve stained with hematoxylin and eosin, while figures 83, 84, 85, 86 and 88 show the normal nerve stained with the silver method for astrocytes.)

The second cell element is the oligodendrocyte (fig. 91), which, according to del Río Hortega, is by far the more numerous in both the brain

and the optic nerve. Oligodendrocytes were first identified by Robertson and more recently and much more fully described by del Río Hortega and by Penfield. They are seen in the optic nerve with ordinary stains and when longitudinal sections of the nerve are studied they are recognized as the well known rows of cells (mostly with small round nuclei, though

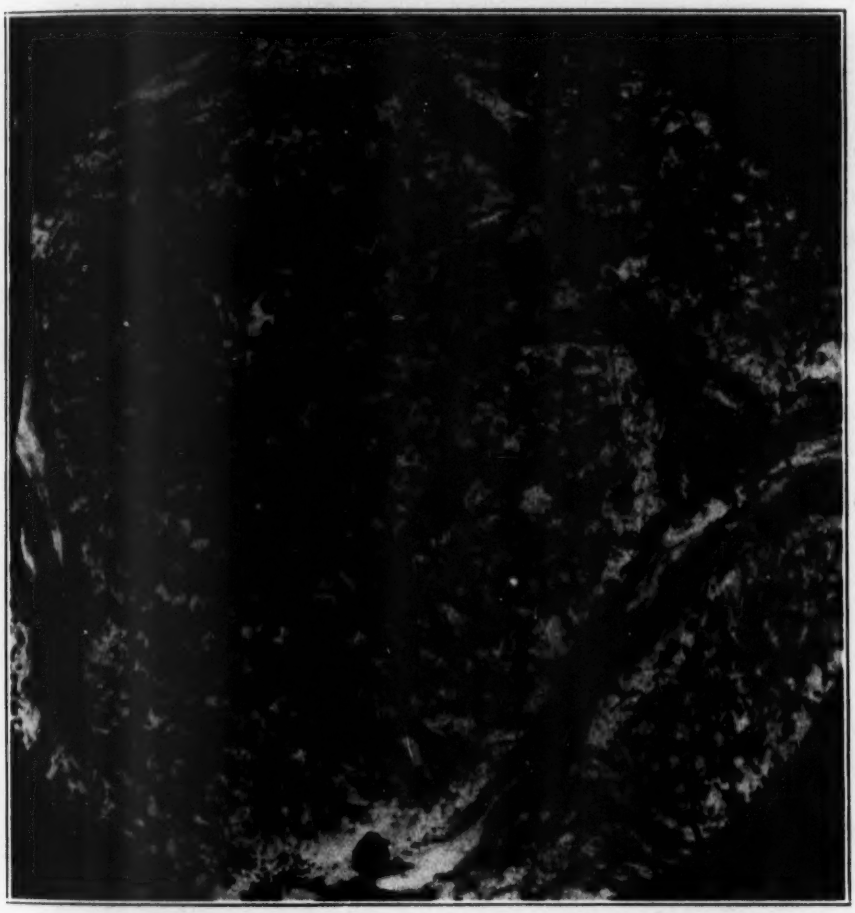

Fig. 86.—Normal optic nerve (× 550). The small black points are nerve fibers surrounded by white halos (myelin sheath).

sometimes oval) which run in parallel columns. With special silver stains, these cells are seen to be round or oval or sometimes quadrilateral in shape, with round or oval nuclei, which appear translucent and are surrounded by a more densely stained protoplasm from which short, curling (sometimes beaded) processes extend (figs. 85, 86, 88 and 91). In my sections many of these cells show only one short process, though

frequently two or more are present. These processes, according to del Río Hortega and Penfield, form an intimate contact with the individual myelinated nerve fibers, encircling or wrapping themselves about

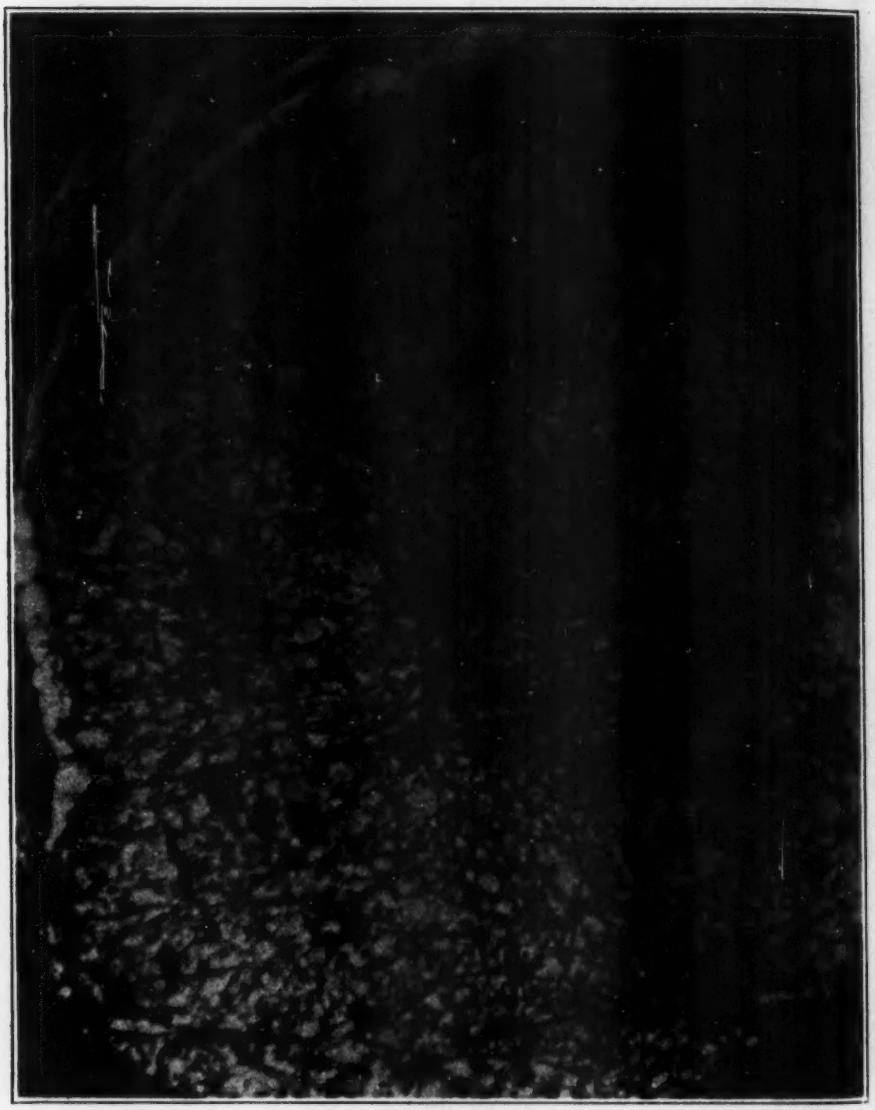

Fig. 87.—Normal optic nerve (phosphotungstic acid stain; × 500). The glial framework is well shown. Note the astrocytes and a few oligodendrocytes. The glial processes are ordinarily not so well shown as they appear here with phosphotungstic acid stain.

them. The specific function of these cells has not been finally determined, though it apparently is related to the elaboration or maintenance of the myelin.

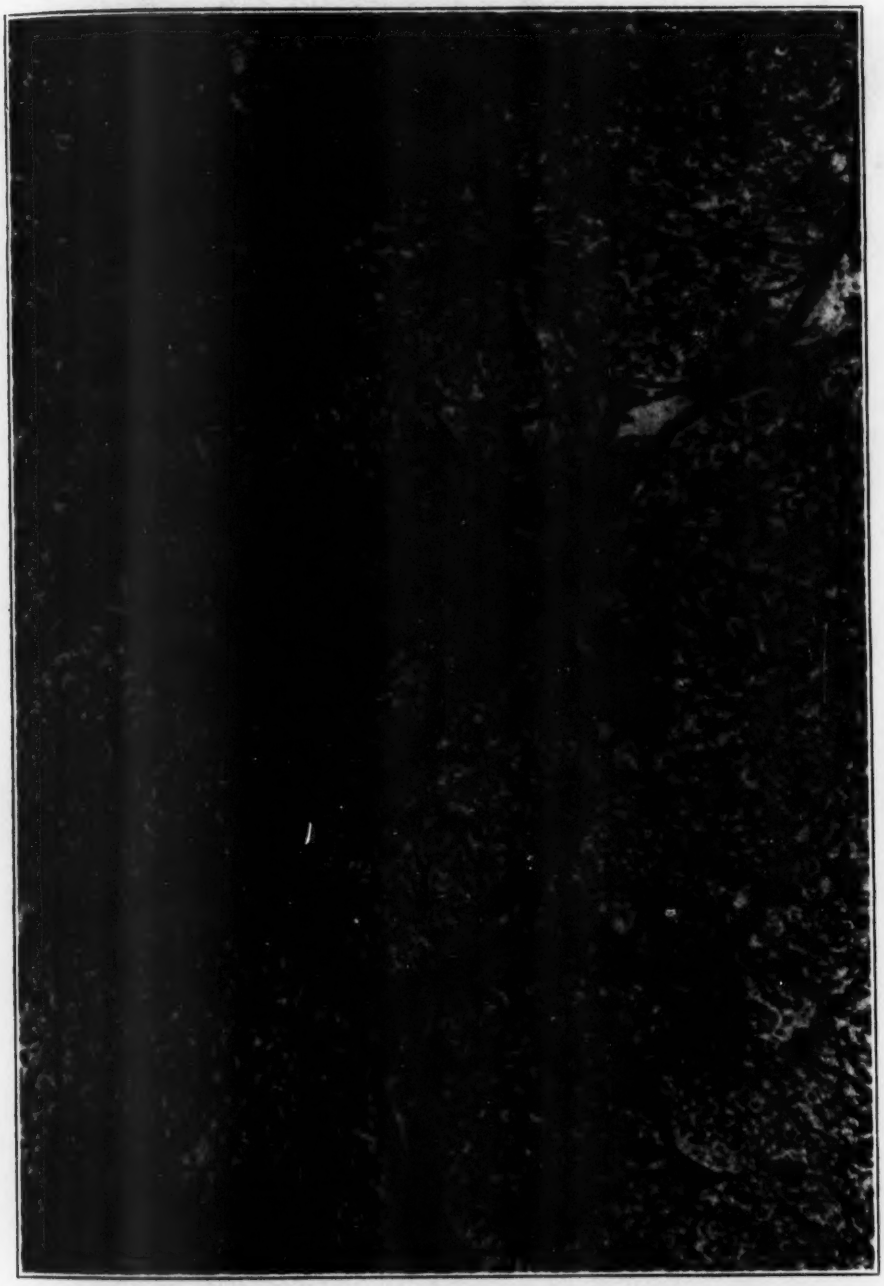

Fig. 88.—Normal optic nerve (Weil-Davenport ammoniacal silver stain; × 500), transverse section. Note the fibrous astrocytes with numerous long fibers which branch and end on connective tissue septums. The glial framework produced by the processes from the astrocytes is well shown. Oligodendrocytes are also seen. The small black points are nerve fibers cut transversely surrounded by myelin sheath (white).

Del Río Hortega maintained that these cells are therefore analogous to the cells of the sheath of Schwann of the peripheral nerves and referred to them as *Brüderzellen*. Cone and McMillan stated: " . . . we have now only presumptive evidence that between them and medullated nerve fibers a synergetic and obligatory symbiotic relationship exists." Their function with relation to maintenance of the myelin,

Fig. 89.—Sections from a normal optic nerve (hematoxylin and eosin stain; × 300). This illustration and figure 90 are shown to bring out the marked contrast with sections of normal optic nerve stained with a silver stain (shown in the preceding illustrations). The lack of detail in these two sections is striking.

however, is in a measure corroborated by the work of Cone and McMillan, who reported that oligodendrocytes have not been demonstrated in the unmyelinated portion of the optic nerve, that is, internal to the lamina cribrosa. They find these cells are present, however, in the nerve head and the retina of animals, such as rabbits, in which the nerve fibers are normally myelinated in the retina for some distance beyond the borders of the disk. While oligodendrocytes show short

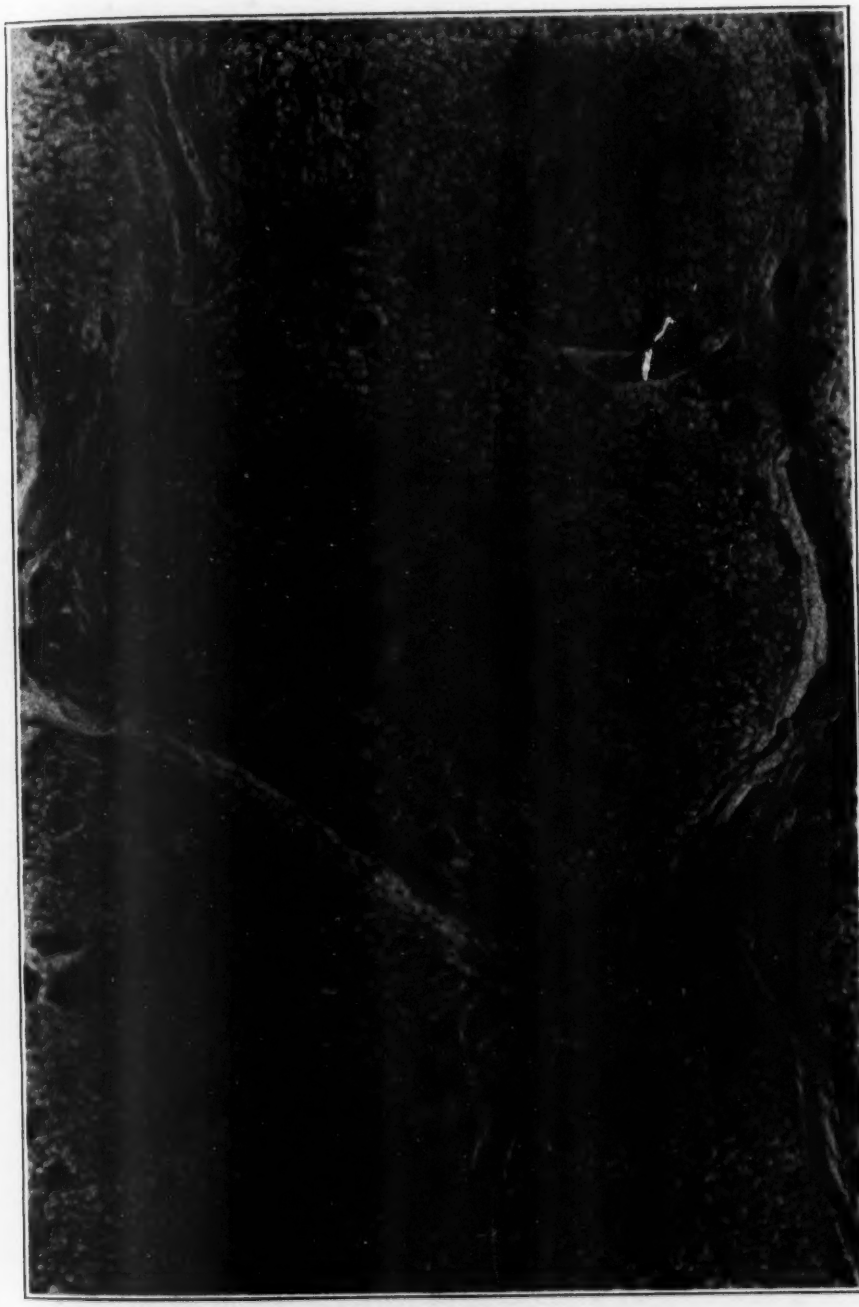

Fig. 90.—High power magnification of the section in figure 89 (hematoxylin and eosin; × 550). Note the large oval cells (nuclei of astrocytes) and smaller round cells (nuclei of oligodendrocytes).

processes extending out from the cell body, they do not, according to Penfield, form long processes or fibers similar to fibrous astrocytes, nor do they show arterial sucker expansions or subpial attachments (feet) which are characteristic of protoplasmic and fibrous astrocytes.

Fig. 91.—Normal nerve, longitudinal section (Weil-Davenport ammoniacal silver stain; × 500). Note the oligodendrocytes, the translucent round nucleus, the heavily stained cell body and the short processes.

Del Río Hortega first described microglia, the third cell element. Microglia cells are sometimes called Hortega cells. They are mesodermal in origin and are much fewer in number than the astrocytes and oligodendrocytes. According to del Río Hortega, they are motile at times.

especially in the presence of inflammatory processes. Their presence in the optic nerve has also been demonstrated by Enriquez. They have small oval or elongated nuclei from which short delicate expansions extend in every direction. They have phagocytic properties and are seen occasionally in sections of normal nerve.

Histologic study of the neuroglia of the normal nerve with the newer methods of staining with silver and gold compounds has proved helpful in the interpretation of these tumors. The technic is long and complicated, requiring frequent repetition before satisfactory results can be obtained. When successful, however, the histologic structure of the normal nerve is revealed in a totally new light. The indefinite ground substance which with ordinary stains is seen surrounding the nerve fibers is with these special stains revealed as an intricate network of fibers (figs. 84, 87 and 88).

Astrocytes and oligodendrocytes have been satisfactorily stained in my sections, but microglia have been more difficult to bring out.

CLASSIFICATION OF TYPES OF GLIOMAS FOUND AMONG TUMORS OF THE OPTIC NERVE

Most authors have made no attempt to classify the particular type of glioma found among tumors of the optic nerve. Verhoeff stated that it is impossible to determine from what the tumors primarily arise but that ultimately they are composed of cells derived from astrocytes. He added, however, that it is best not to attempt to classify them on an embryologic basis.

Bailey and Cushing, in their classification of gliomas of the brain, suggested that many of the varied manifestations of these growths may well apply to those of the optic nerve, since the nerve arises from the same primary neural elements. They did not attempt in their text, however, to classify 11 gliomas of the optic chiasm reported by Martin and Cushing, since the ". . . histogenesis of the interstitial tissue of the region is too imperfectly known to allow proper evaluation of their tumors." The latter authors in their important contribution stated: ". . . at this time the least that can be done is to designate as gliomas those tumors of the central nervous system which show glial fibers with proper selective stain."

Grinker (1930) stated that all the tumors classified as gliomas affecting the optic nerve seem to be definitely spongioblastomas of the unipolar and bipolar type and suggested that more specific staining methods may clear up this point. His conclusions, however, appear to be based on studies of cases reported in the literature by others, most of which, according to his statement, were made with the use of ordinary nuclear stains and teased tissue preparations.

Lundberg (1935), using special differential silver stains, such as Hortega's, and various modifications, such as Fincher's stated that all the tumors he examined were oligodendrocytomas, with one exception —an endothelioma. He found that the cells of the tumors of the optic nerve he studied showed a considerable polymorphism. Mitosis was observed, but only to a slight degree. In all the tumors he found a few astrocytes and cells similar to astrocytes, which he thought were transitional forms between astrocytes and oligodendrocytes. He considered the tumors to be oligodendrocytomas, that is, formed by cellular elements resembling those of the oligodendroglia. This author concluded that the genesis of gliomas of the oligodendrocytoma type is to be sought in a process which prevents the more or less developed neuroglial cells from assuming their normal position in relation to the nerve fibers.

Mehney (1936) reported 3 primary tumors of the optic nerve which were diagnosed as spongioblastomas, unipolar in type. Bueno and Llombart reported a glioma of the oligodendrocytoma type (cited on page 996 of this article). Globus described the tumor in the case reported by Goldstein and Wexler as a "spongioneuroblastoma." Schreck (1938) recorded a case of glioma of the optic nerve in which he stated that the cells showed considerable polymorphism but that they were all of the glial type. Oligodendrocytes predominated, and the cells of the astrocyte type were noted occasionally. There was no palisade arrangement.

Busch and Christenson, in the case reports cited in my review of the literature, stated that the tumors resembled a spongioblastoma of the brain stem. The most typical cell elements were the long cells, "oligodendrocytes or spongioblasts," but the round cell type was also present, associated with glial fibers.

Bailey and Herrmann (1938), in the case history cited on page 1002, in commenting on the gliosis of the optic nerves stated: ". . . the glial scar was composed principally of piloid astrocytes."

The tumors herein reported, as noted, were made up of astrocytes and oligodendrocytes, but the astrocytes were definitely the predominant cell type. Since the oligodendrocytes are far more numerous than other cells in the normal nerve (75 per cent according to Enriquez), any general abnormal proliferation of the cellular elements of the nerve would be likely to show them increased proportionately. In the tumors here considered, however, the astrocytes were enormously increased and their fibrous expansions greatly multiplied; so they are classified as astrocytomas.

In areas of the nerve adjacent to the main tumor mass, where the new growth was less advanced, the cellular detail differed considerably. In these areas the astrocytes and oligodendrocytes appeared much like those of the normal nerve, though much enlarged.

Multinucleated groups of cells were frequently encountered in the tumor of the nerve stem, which I have interpreted as amitotic division of the neoplastic cells. These multinucleated groups appeared in both astrocytes and oligodendrocytes. The expansions from the astrocytes were much coarser and thicker than those normally seen and often could be traced for long distances (figs. 79 and 80). The astrocytes were often branched in atypical fashion, frequently only three main processes extending from the cells. As the tumor advanced, fiber formation became so pronounced that much of the cellular detail was lost or difficult to bring out. Fiber formation was the outstanding characteristic of the new growth, both within the nerve stem and within that portion of the tumor which had invaded the sheath. The cell body showed the typical outlines of swollen or giant astrocytes, though numerous oligodendrocytes were also present. The appearance, therefore, was one of a general abnormal proliferation of astrocytes and oligodendrocytes, with astrocytes definitely predominating.

In the areas where the tumor had invaded the sheath and where the glial fibers were especially densely packed within the nerve stem, the character of the cell body was somewhat altered. In these areas the typical multiple expansion or spider contour was not so evident, and oligodendrocytes were rarely seen. These variations, however, were interpreted as atypical forms due to the changed or abnormal environment. The tumor type cell was certainly not that of a bipolar spongioblast, as reported by others, though, as noted previously, some of the cells resembled them as well as the unipolar pear-shaped type.

As pointed out by Bailey and Cushing, all the varied types of gliomas found in the brain may have their counterpart in tumors of the optic nerve, since the retina and nerve are but an expanded portion of the brain. At the present time an insufficient number of studies have been made with modern differential staining methods to attempt to classify all of these tumors on this basis. Recently reported cases, however, indicate that definite progress is being made in this direction.

RECKLINGHAUSEN'S DISEASE

Recklinghausen's disease is best known as a multiple tumor syndrome which involves the peripheral nerves. It is congenital in origin, though the lesions are progressive. The tumors which characterize the disease are frequently seen in and beneath the skin, scattered over various parts of the body, and are commonly referred to as neurofibromas. These tumors, however, are at times found in the cerebrospinal nerve trunks and may also involve the nerves of the sympathetic system.

Recently, lesions within the brain, such as areas of gliosis, gliomas and meningiomas, have also been reported in association with the more

typical peripheral signs. Soft nodules in the skin, known as molluscum fibrosum, and café au lait patches may accompany the more obvious tumors of the nerves, or they may be the only visible evidence of the disease. At times there is a diffuse, soft overgrowth of connective tissue surrounding the fine terminal nerve branches, known as elephantiasis neuromatodes. Solitary neurofibromas of the nerve trunk may also belong in this category, though many of the solitary tumors have a somewhat different histologic structure and, according to Penfield, are classified as perineural fibroblastomas. This type, however, has also been observed in Recklinghausen's disease.

Multiple swellings occur at times on the more superficial nerve trunks known as "plexiform neurofibromatosis." The upper eyelid and region about the orbit and temple are common sites of these growths. The nerves of the orbit as well as the ciliary nerves within the eyeball may become affected.

Involvement of the nerves of the choroid, ciliary body and iris is usually accompanied by enlargement of the globe, or buphthalmos. More recently defects in the bony structures, such as scoliosis of the spine, deformities of the long bones and defects in the bony orbit, have been added to this already complex symptomatology. The bony lesions probably arise indirectly due to involvement of adjacent nerves (Brooks and Lehmann), especially tumors of the roots of the spinal nerves, though the nerves within the bone may also be affected.

Case reports reveal that tumors of most of the cranial nerves have at times accompanied the more common peripheral lesions, bilateral involvement of the acoustic nerves being an outstanding example. The olfactory and optic nerves usually have been considered exempt from the disease, since they are structurally different from other nerves. The optic nerve is not a true nerve but is a fiber tract comparable to intercerebral pathways within the brain. The supportive tissue and enveloping sheaths likewise differ from those of peripheral nerves. There is evidence available, however, which indicates that the optic nerve is no exception and that tumors which affect it may belong in this classification.

It is beyond the scope of this paper to enter into a detailed discussion of the histologic picture of the varied lesions associated with Recklinghausen's disease. Brief reference to views of a few outstanding authorities, however, will be given, since some knowledge of the nature of these growths is essential to an understanding of the possible role of tumors of the optic nerve in this syndrome.

Von Recklinghausen expressed the belief that the tumors were chiefly fibrous in nature and that they arose from the connective tissue elements of the nerves.

In his text, "Neoplastic Diseases," Ewing stated: "A satisfactory classification of these tumors is difficult, owing to the complex structure

of the nerve trunks and the uncertainty of the source of the supporting cells which accompany nerve fibers, such as the cells of Schwann—the neurilemma, the endoneurium, the lymph sheaths of the nerve trunks, all of which participate in the tumor growth."

The lesions have been classed under the generic term "neurofibromatosis." [8]

In a discussion of the cell changes found in Recklinghausen's disease, Penfield referred to the varied types of lesions which may be encountered in some examples of this disease. He emphasized the fact that "the tumors which affect the nerves, meninges, and central nervous system are similar to those which may arise from these tissues under other circumstances." He stated that the neurofibroma is made up of adult tissue and added:

"The perineurial fibroblastoma is a growth of fibroblasts which preserve their peculiar differentiated characteristics. The gliomas, such as were present in a case reported by Penfield and Young, were made up of differentiated cells (astrocytomas and ependymomas), while the meningeal tumors were composed of fibroblasts which preserved the habitual characteristics of meningeal fibroblasts."

A controversy has arisen among pathologists concerning the histogenesis of some of these tumors. Verocay, Antoni, Masson and others have stressed the importance of the part played by the cells of the sheath of Schwann as the original source of tumors of the peripheral nerves, while Mallory and Penfield have emphasized the fibrous nature of the growths. Penfield and Young (1930) stated that they "find no difficulty in subscribing to the doctrine that the congenital defect may be in the sheath of Schwann, although as yet there is no proof histologically."

Bailey and Herrmann (1938) stated that they are skeptical of the schwannian theory of the origin and nature of any of the tumors of peripheral nerves. They concluded from an exhaustive histologic study of the tumors in 2 remarkable cases in which there was extensive involvement of the peripheral and cranial nerves as well as of the meninges that the cells of Schwann play a minor and secondary role in the production of tumors of the peripheral nerves, though they admitted that the origin of the tumors still remains in doubt. Penfield and Young expressed the view, which is also advanced by others, that in Recklinghausen's disease an irritating or a stimulating influence is exerted on the various tissues, causing hyperplasia in them, and superimposed on or sequent to this effect is the appearance of neoplastic

8. Some of the lesions associated with this syndrome are not, in a strict sense, a part of the disease described by Recklinghausen, but the term is here used to cover all the varied manifestations which at times accompany the more classic signs which he described.

growths in these cells. This suggests a congenital defect in the nervous system in some way capable of producing the necessary irritation of adjacent tissues.

The search for the particular congenital defect which might be responsible for such widespread lesions as characterize this disease has been a lively one, judging from the volume of literature bearing on this subject. Since Harrison (1924) has demonstrated that the Schwann cell arises in the neural crest and later migrates out along the course of the peripheral nerves, a working hypothesis has been supplied whereby the origin of some of these tumors might be attributed to a congenital defect in the neural crest.

Oberling's contention that the leptomenix (pia-arachnoid) is also a derivative of the neural crest suggests that some of the associated lesions of the central nervous system, such as tumors of the meninges, which form a part of the Recklinghausen syndrome, might also be explained by a similar congenital defect. His views have not received general endorsement, though Bailey and Cushing remarked that evidence is accumulating from embryologic, pathologic and experimental studies that meningioblasts which form the leptomenges are also migratory cells from the ganglionic crest.

Tumors arising in the stem of the optic nerve, such as the gliomas here considered, can hardly be associated with maldevelopment of the neural crest, since the optic nerves are derived from a wholly different part of the neural ectoderm.

Bailey and Herrmann remarked that if one attempts to account for tumors of the central as well as of the peripheral nervous system on the basis of maldevelopment, the medullary plate and also the neural crest would be involved. These authors, therefore, questioned the assumptions of others who have attempted to link these tumors to some common embryologic defect. They stated in this connection: "If the neuroectodermal structures are malformed, associated mesodermal structures, lacking the proper stimulus, will also not develop properly, and thus possibly also be liable to neoplastic change." They added: ". . . the whole development of inductive embryology of Spemann and his school indicate that the orderly development of the body is due to a concantenation of mutually interacting forces, the derangement of any one of which will deviate the orderly unfolding of the rest."

Ida Mann, referring to the phakomatoses and especially to Recklinghausen's disease, stated, ". . . the tumors tend to be associated with peripheral nerves," though she included tumors of the optic nerve and buphthalmos in her tables. She expressed the belief that the defects are pure aberrations of a hyperplastic nature and that they bear no relation to normal embryonic stages. She wrote: "They imply a lack of

stability and a general degeneration in the stock so that the initial organizers fail to produce a perfect organ but, instead, one blurred and aberrant, with enough vitality to begin but not to end normally." She further pointed out that such abnormal development continues after birth and generally throughout life.

Fuchs, in his text, referred briefly to Recklinghausen's disease, stating that it is made up of a series of changes which are congenital for the most part, yet never occur all at the same time. In addition to the more common and well known signs, he added tumors of the optic and acoustic nerves as well as hydrophthalmos.

Though gliomas and meningeal tumors as well as neurofibromas and perineural fibroblastomas appear associated at times in Recklinghausen's disease, Penfield remarked that it does not necessarily follow that they arise from the same blastodermic layers. He further emphasized the fact that the type cell of all three of the tumors of this nature which were found in a case reported by Penfield and Young was not embryonic but was in each instance well differentiated.

Since tumors associated with this disease present such varied histologic characteristics and are so widely disseminated throughout the central and peripheral nervous systems, it seems plausible to assume that the cause of the disease must reside within the nerve cells and fibers, while proliferation of the supportive elements of nerve tissues, that is, meninges, glia, endoneurium, perineurium, epineurium and neurilemma (sheath of Schwann), may be a purely secondary process which is brought on by subsequent degeneration of the affected nerve elements. The appearance of the tumors which were found along the course of the nerves in the orbit (fig. 63) in case 3 of this series suggests that atrophy and disappearance of the nerve fibers had been followed by a tumor-like mass in the surrounding supportive tissues.

Penfield has pointed out that the tumors of Recklinghausen's disease in general have an appearance more like a reaction about nerve fibers than a neoplastic growth.

RELATIONS OF TUMORS OF THE OPTIC NERVE TO RECKLINGHAUSEN'S DISEASE

A Review of the Literature.—If the underlying factor which is responsible for tumors of Recklinghausen's disease is some defect in the sheath of Schwann, it would appear that the optic nerve, which is a cranial nerve and lacks the sheath of Schwann, would not participate in this disease. Isolated case reports in which the two conditions coexisted have appeared from time to time, however, and attention has been directed to the significance of this fact. In the more exhaustive surveys of the subject of primary tumors of the optic nerve, writers

have discussed this possible relation only to discard the theory in most instances or at best to say that it is based on insufficient evidence.

Michel (1873) was apparently the first to record a case of this nature, reporting a tumor of the optic nerve associated with elephantiasis of one leg. The tumor consisted of a glial hyperplasia of the chiasm and right optic nerve (fig. 71). It was discovered by accident at autopsy, the patient (a boy of 16) having died from septicemia, the result of an infected tumor (elephantiasis) of the leg. No ocular studies had been made, and the author regarded the association of the lesions as probably accidental.

Westphalen (1887) reported the occurrence of Recklinghausen's disease in a woman of 35, with typical multiple tumors of the skin and peripheral nerves. Autopsy revealed a tumor-like enlargement of the optic nerve just before its entrance into the optic foramen. No ocular symptoms were recorded in the clinical history, and no histologic study of the enlargement of the optic nerve was reported. There was an associated psammofibroma of the dura. Sarcomatous degeneration of a neurofibroma of the tibial and the peroneal nerve was reported, with metastasis to the lungs.

Early recognition of the association of tumors of the optic nerve and multiple tumors of other nerves has been erroneously attributed to Goldmann (1893). In his frequently quoted paper, this author stated that multiple neuromas may involve not only the peripheral nerves but the cerebrospinal and sympathetic nerves. He specifically stated, however, that the olfactory and optic nerves are not involved. He remarked that neuromas of the optic nerves may show a structure homologous with that of other multiple neuromas, though he did not report such a case. Since he expressed the belief that tumors of the optic nerve arise from the connective tissue elements of the nerve, he regarded their structure as similar to tumors of the peripheral nerves.

By far the most important early contribution to this subject was that of Emanuel (1902) concerning the relation of tumors of the optic nerve to elephantiasis neuromatodes, a form of Recklinghausen's disease. He developed a theory which was based chiefly on a few case reports in the literature, since he had actually observed no case of this nature. He cited a case of Sattler (1892), that of a glial tumor of the nerve which eventually involved both nerves. The child had no general manifestations of Recklinghausen's disease, but a brother, the father and a grandfather had typical peripheral lesions, such as café au lait spots and numerous mollusca fibrosa. Emanuel found 4 other cases in the literature in which the second eye became blind before or after operation on the fellow eye for a tumor of the optic nerve. He cites 10 cases in which it was found at autopsy that more than one portion of the nerve showed tumor formation, and he also referred in some detail to the reports of

Michel and Goldmann, which have already been briefly reviewed. He likewise cited the case reported by Westphalen. While Emanuel, himself, admitted that this case was the only one he had found in which generalized neurofibromatosis was present, curiously enough he nevertheless sensed the possible significance of this relation, and his conclusions are the more remarkable for this fact. He recognized the nature of certain gliomas of the optic nerve, reporting 2 cases unassociated with Recklinghausen's disease at the end of his paper, but he stated that it is wise to limit the term to tumors confined within the pial sheath. He apparently regarded all other tumors of the nerve as manifestations of elephantiasis neuromatodes, for he commented: "They resemble tumors of the connective tissue of other nerves; since they may be multiple, they show the same variety of cellular structure without reference to relative malignancy, and, lastly, their later course may resemble that of secondary malignant neuroma."

Since Byers (1901) erroneously regarded all primary intradural tumors of the optic nerve as representing some phase of fibromatosis, he placed them in the category of false neuromas, stating that "an overgrowth of the connective tissue structures was responsible for the tumefaction of the nerves." While admitting a certain want of clinical association between these tumors of the optic nerve and false neuromas affecting other nerves of the body, he mentioned 1 case of Prudden (cited by Goldmann) in which there were multiple fibromas associated with the tumors of the optic nerve. He concluded: ". . . add to this certain points of clinical resemblance between the two forms of tumor and we feel that the changes show that they are at least intimately related if, indeed, they are not identical in character." While Byers' reasoning may have been based on a false premise, his conclusions ultimately may be proved correct.

Alexis Thomson (1900), in his excellent monograph, "On Neuroma and Neurofibromatosis," only briefly mentioned the optic nerve, but he definitely stated: "Tumors of the optic nerve may occur in association with Von Recklinghausen's disease." He cited 4 case reports in his tables, namely, those of Westphalen, Serres, Soyka and Prudden and Satterthwaite. In the case of Soyka multiple tumors of the brain and cerebellum were present in addition to peripheral lesions. These citations have received little attention.

Hudson's article (1912) on primary tumors of the optic nerve refers to the claims of the others regarding the association of these tumors with neurofibromatosis. He stated that Goldmann (1893) was the first to suggest that these tumors were a manifestation of generalized neurofibromatosis. With regard to the suggestion put forward by several authors, among them Byers, Emanuel and Strube, Hudson stated that

he endorsed the point of view of the last, who regarded such multiple lesions as a "development, side by side, of two processes which both may be considered as developmental anomalies, conceivably as a result of a common stimulus."

Fehr (1913) reported 2 cases of Recklinghausen's disease with ocular symptoms. In 1 case he stated there was no evidence of damage to the optic nerve. In the second case the symptoms suggested a possible tumor of the optic nerve, but at operation (Krönlein method) no tumor could be found by palpation of the nerve by the finger. Fehr expressed the opinion, however, that a small tumor could be overlooked, though it might be large enough to be responsible for the symptoms.

Pincus (1913) reported a case of Recklinghausen's disease in which the symptoms and a study of the visual fields indicated bilateral optic neuritis. The author noted the possibility of there being a tumor of the brain, though there were no other symptoms of such. He also noted the possibility of a "neurofibroma" of the optic nerve, adding that definite proof in such cases must await histologic examinations.

Christin and Naville (1920) reported 4 cases of neurofibromatosis with involvement of the central nervous system. In 1 of these cases, in which ophthalmologic examination had indicated optic neuritis, autopsy revealed numerous neoplastic nodules in the brain, one pressing on the right optic nerve. In 1 of the other cases complete blindness had existed since childhood, and the authors stated that ophthalmoscopic examination demonstrated proliferation of the connective tissue of the retina and optic nerve, that is, the existence of a "neurofibroma of the optic nerve and retina." The ophthalmoscope showed much the same picture in another case, but in neither could the ocular condition be considered as a proliferating retinitis nor as "glioma of the retina." The authors asserted that they have found no other cases reported of this type except that of Pincus, in which it was suggested a "neurofibroma" of the optic nerve might be present.

Parker (1922) reported a case of Recklinghausen's disease with involvement of the optic nerve (also reported by Benedict, 1923).[9] The tumor was a "typical dural endothelioma." There were numerous tumors of the peripheral nerves, which proved to be neurofibromas, and tumors of the spinal cord, which were found to be dural endotheliomas. The patient was observed at intervals for eight years after removal of the tumor of the orbit, and during that time the symptoms indicated a progression of the intracranial and spinal lesions. Operation later revealed an intracranial meningioma too extensive to permit removal (1928) and a new tumor in the cord. The patient died two years

9. I have had the opportunity of studying some of the sections of this tumor (fig. 5) as well as others in Dr. Benedict's collection.

later, and postmortem study of the brain and spinal cord was reported by Kernohan and Parker (1932). Numerous meningiomas and two distinct gliomas (astrocytoma and ependymoma types) of the cord were found as well as syringomyelia, neurofibroma and fibroblastomas perineural of several cranial nerves and dorsal roots. No further tumor formation was found in the intracranial portion of the optic nerves, nor was a recurrence of the tumor in the orbit reported. Autopsy did not indicate any meningeal tumor in the region of the optic nerves, so it would appear that the dural endothelioma of the sheath of the optic nerve was a primary lesion, independent of the multiple intracranial growths. The tumors of the spinal roots involved the dorsal roots only, the anterior roots being unaffected.

Verhoeff (1922) gave a brief discussion of the relation of these tumors to generalized neurofibromatosis. He stated: ". . . since these tumors of the optic nerve in their gross appearance bear considerable resemblance to neurofibromas of the peripheral nerves, it is not surprising that attempts have been made to prove that they were of the same nature or were dependent upon similar causes." Further, he added: ". . . the data presented by Goldmann and Byers were based chiefly on the assumption that tumors of the optic nerve were composed primarily of mesoblastic tissue, and since we know these tumors are composed essentially of neuroglia their argument falls to the ground." Referring to Emanuel's theory, he remarked: "If it were correct it would seem that among the numerous cases of glioma of the optic nerve that have been reported in the literature, in at least one case, the two conditions should have co-existed." He admitted, however, that "the possibility still remains that the same influence which causes supporting tissue of a peripheral nerve to proliferate in the form of a fibroma, may cause the supporting tissue of the optic nerve to proliferate in the form of a glioma." In a later résumé (1932) Verhoeff commented that in possibly 4 cases "a glioma of the optic nerve has been associated with Von Recklinghausen's disease." He added, however, "it does not follow they are related to fibroma of the peripheral nerves except to the extent that both may be dependent upon some congenital developmental anomaly."

Wiegmann (1923) reported the case of a man 44 years of age in which a number of abnormalities and, in addition, pigmented areas and numerous cutaneous tumors typical of Recklinghausen's disease were present. Vision was much reduced, and ophthalmoscopic examination showed bilateral atrophy of the optic nerve. At autopsy sections from the optic chiasm and the left optic nerve showed a sclerotic thickening similar to that of the peripheral nerves in one of the affected extremities.

Steurer (1922) reported 2 cases of Recklinghausen's disease in which the acoustic nerve was involved. In both cases there were visual

disturbances, and 1 of the patients suddenly became completely blind shortly before death. In the latter case a tumor the size of a pea was found on the right optic nerve, apparently originating in the sheath. No histologic description of this tumor was given, as the author was interested in changes in the inner ear. In the other case a tumor of the base extended to the optic chiasm but did not involve the optic nerve.

Von Hippel (1925) discussed the subject of tumors of the optic nerve and generalized neurofibromatosis at some length, citing a number of references to cases reported. He stated: ". . . it is evident that proof sufficient to support the theory of Emanuel, to which Byers also subscribes, is not yet available, and it has been repeatedly challenged."

Martin and Cushing (1923), in their excellent paper, "Primary Gliomas of the Chiasm and Optic Nerve," reported 7 cases of glioma of the optic chiasm. In 1 of these, that of a girl 6 years of age, there were small pigmented patches on the left side of the body, and in another (case 7) there was a definite generalized neurofibromatosis. In all of these cases the intracranial portion of the optic nerve and the optic chiasm were involved, and in 1 case the growth involved the orbital portion of the nerve up to the papilla. These authors emphasized the fact that "it is well known that multiple cranial nerve tumors may accompany outspoken examples of Von Recklinghausen's disease, but of all the nerves the optics are perhaps the least often involved in the process, while the acoustic nerves are more commonly affected." They also stated that "one is forced to consider the possibility that there may be gliomas of different types—relatively malignant and relatively non-malignant varieties of what Hudson terms 'gliomatosis' " and, to quote further, ". . . it is necessary to mention that the neurofibromatosis of Von Recklinghausen's disease, a comparatively benign process, *may have* been the underlying factor in some, perhaps in many, of the recorded cases with a particularly favorable outcome!" These authors draw some pertinent and important conclusions for ophthalmologists; namely, that "in such cases we have an explanation for some of the obscure cases of primary optic atrophy so often attributed to retrobulbar neuritis. Certainly a primary atrophy in cases of generalized neurofibromatosis or even those with slight manifestations of this malady will rest under suspicion of having a gliomatous process in the chiasm or its adjacent nerves. Suspicion will also be aroused when there is an obvious swelling of an atrophic nerve head without evidence of increased intracranial pressure."

Van der Hoeve (1925) recorded the history of a woman aged 37 who had had reduced visual acuity since childhood and who had definite peripheral neurofibromatosis. Intracranial exploration, with removal of the roof of the optic canal, revealed marked enlargement of the optic

nerve, and the author thought that the involvement was probably bilateral. No biopsy specimen was taken, but he regarded the growth as "neurofibromatosis of the nerve." One eye was subsequently (1933) enucleated, since it was blind, but histologic study had not been made at the time of the report. The author stated: ". . . it is highly probable that in cases of Von Recklinghausen's disease, tumors of the optic nerve are more frequent than we think." He therefore stressed the importance of roentgen studies of the optic foramen, which proved to be much enlarged in his case.

Abelsdorff (1928), in his discussion of glioma of the optic nerve, considered as erroneous Emanuel's conclusions in regard to the relation that exists between tumors of the optic nerve and Recklinghausen's disease. In the first place, Abelsdorff expressed the belief that it has not been proved that multiple tumors arise in the optic nerve, and in the second place that the optic nerve, like the olfactory nerve, is not involved in cases of Recklinghausen's disease.

Holmström (1928) reported the occurrence of Recklinghausen's disease in sisters, 4 and 5 years of age. The older girl showed typical tumors of several peripheral nerves; the younger sister showed only pigmentation on one shoulder with no true tumors. Both children had exophthalmos of the right eye, some diminution in vision and pallor of the optic disk. Roentgenographic examination of the orbit showed that the right optic canal was definitely wider than the left in both instances. The author considered this as evidence that there was a tumor of the optic nerve in each case, though he cautioned that histologic examination would be necessary to verify this conclusion. The condition was hereditary, the father of the girls having numerous tumors on his face and body.

Schnyder (1928) reported a case of multiple tumors, combined with a neurofibroma of the right ninth intercostal nerve, a neurofibrosarcoma of the right third cervical nerve which destroyed the third cervical vertebra, a glioma of the infundibulum and diffuse gliosis of both optic nerves. He expressed the opinion that there are cases in which there is a congenital disposition of the neuroglia to tumor formation. In such cases glioma and gliosis may be found in various portions of the central nervous system, and neurinoma of the peripheral nerves and the multiple occurrence of such tumors cannot be attributed to metastases.

Cushing (1930), in an article on the chiasmal syndrome, included cases of glioma of the optic chiasm, which, he stated are "less well known" than gliomas that involve the optic nerve in its intraorbital course. He stated that in his full series of 18 cases of this type, including those reported in 1923, there were 6 in which there was evidence of

Recklinghausen's disease. He described 2 illustrative cases, in 1 of which there were typical cutaneous manifestations of this disease.[10]

Katzenstein (1932) reported a case of multiple tumors in the central nervous system and small cutaneous nodules. There was diminution of vision, but no mention is made of involvement of the optic nerve in the detailed pathologic description of the various tumors. Visual symptoms were attributed to the tumors of the brain. The acoustic nerve was involved. It seems likely the visual defects in this case were due to glial changes in the optic nerves.

Goldstein and Wexler (1932) reported a case of tumor of the optic nerve associated with multiple neurofibromas of the peripheral nerves. No failure of vision had been noted during life, but at autopsy the left optic nerve was found to be "uniformly thickened in its entire course." Histologic study of the left optic nerve showed a tumor mass with two predominating types of cells, which were "unlike those usually described for glioma of the optic nerve." Dr. Joseph H. Globus examined the specimens and considered that the larger cells represented neuroblasts and the smaller type spongioblasts. He suggested the diagnosis "spongioneuroblastoma" for this tumor. Goldstein and Wexler wrote: "Earlier authors (Goldmann, Byers, Emanuel) held that optic nerve tumors were mesodermal in origin and considered most of these tumors fibromatous in nature and probably related to neurofibroma. In spite of our knowledge that gliomas are glial in nature, and therefore ectodermal, it is significant indeed if a glioma-like tumor of the optic nerve is demonstrated beyond question in a case of generalized neurofibromatosis." They added the significant comment, ". . . the literature is not lacking in optic nerve tumors in neurofibromatosis, but up to the present time apparently none has been considered authentic."

Bueno and Llombart (1933) reported pigmented areas on the body, such as are observed in Recklinghausen's disease, of a child 6 years of age; however, there were no other cutaneous symptoms. Symptoms of tumor of the optic nerve necessitated operation. The tumor was removed, and histologic examination showed it to be a glioma of the oligodendrocytoma type. A detailed histologic description is given.

Hartmann (1933) reported tumors of the optic nerve occurring in 3 patients with definite symptoms of Recklinghausen's disease. All the patients showed areas of pigmentation and cutaneous tumors characteristic of this disease. In 2 of the 3 cases diagnosis of tumor of the optic nerve was confirmed at operation or autopsy and the histologic nature of the tumor determined. One was considered to be a fibrosarcoma or, according to Pfauque, a "polymorphous meningoblastoma";

10. This case (B. S.) was also recorded by Bailey and Herrmann, with autopsy reports.

the other was classed as a neurofibroma. In the third case the left eye was blind and there was exophthalmos. Roentgenograms showed enlargement of the optic canal on the left side, similar to that observed in the other 2 cases in which the diagnosis of tumor of the optic nerve was confirmed. The diagnosis of tumor of the optic nerve was made in this case, but operation was not performed.

Foerster and Gagel (1934) reported a case of Recklinghausen's disease "with cutaneous neurofibromas and pigmented spots and diffuse proliferation in the central nervous system of 'Schwann' cells or immature forms of these cells." The optic chiasm was involved, and the cells were numerous in both optic nerves. The authors attributed the marked diminution of vision observed clinically to the extension of the process to the optic nerves.

Fleischer (1934) noted that glial tumors (gliomatosis) of the optic nerve are not always confined to the intraorbital portion of the nerve but may extend into the intracranial portion, even to the chiasm. A number of cases of bilateral tumor have been reported in which the chiasm was involved. The author has observed 2 such cases, in 1 of which autopsy was recently performed. The patients in both cases were children, the child in the latter case being a girl 3½ years of age. In this case autopsy showed bilateral tumor of the optic nerve extending into the optic chiasm. The tumor was of the glial type, which the author designated a "gliomatosis." In this case there was also generalized neurofibromatosis (Recklinghausen's disease), which was hereditary, with numerous nodules on the peripheral as well as on the sympathetic nerves and foci of gliomatosis in the central nervous system. The author stated that the simultaneous occurrence of tumors of the optic nerve and generalized neurofibromatosis is of definite significance. Since the tumor of the optic nerve in his case was histologically the same as tumors observed in other cases without generalized neurofibromatosis, Fleischer expressed the opinion that "it must be concluded that optic nerve gliomas are homologous to the nerve tumors and cutaneous lesions of Von Recklinghausen's disease, and to the lesions of the central nervous system sometimes observed in this disease." He stressed the fact that the "manifestations of Von Recklinghausen's disease may be limited to a single portion of the nervous system—as the optic nerve, central nervous system, a group of peripheral nerves on the skin."

Lundberg (1935) referred to Emanuel's presentation of the relation between tumors of the optic nerve and elephantiasis neuromatodes. In discussing the cases cited in his own review of the literature, he stated that there were 8 cases in which association of the tumor with generalized neurofibromatosis was noted. He remarked, however, that he had never seen any evidence of Recklinghausen's disease in the cases of tumor

of the optic nerve which he personally studied, but he added that it is not impossible that there is a relation between the two conditions. He commented that most authors have espoused the point of view of Verhoeff, namely, that "the theory is founded upon insufficient evidence but cannot be dismissed as impossible." In discussing the histologic nature of tumors of the optic nerve (referred to on page 984), he offered the suggestion that though primary intraneural tumors of the optic nerve originate from the cell element of the neuroglia and Recklinghausen's tumors from Schwann cells there is no basis for assuming a close relation between the two diseases. He referred at length to del Río Hortega's claim that the oligodendrocytes of the neuroglia and Schwann's cells are homologous cells or *Bruderzellen,* but apparently felt that that author has not presented sufficient evidence to substantiate this.

Shapland and Greenfield (1935) reported a remarkable case in which there were numerous tumors involving the brain and cord and the cranial and peripheral nerves. There was complete loss of vision in the left eye with exophthalmos. The vision in the right eye was also reduced and later lost entirely. There was bilateral deafness, due to tumors in the cerebropontile angles, and also evidence of involvement of other cranial nerves, especially the third. There was a small area of "soft bluish skin" in the lumbar region, and a "flat pad of tumor" was found under the scalp. At autopsy these proved to be neurofibromas. There were tumors of three kinds in the central nervous system—meningeal psammomas, neurofibromas on the roots of the spinal and cranial nerves and gliomas in the cord and right frontal lobe. One of the meningeal psammomas involved the sheath of the left optic nerve, and the nerve itself could be seen as a "flattened band in which the connective tissue trabeculae were considerably thickened" and surrounded by a psammomatous tumor. They stated that "the tumor of the optic nerve sheath may have arisen by extension from a similar growth in the middle cranial fossa" and that ". . . an explanation for the association of these three types of tumors is a problem which appears insoluble in the present state of our knowledge."

Schwartz (1936) reported the occurrence of a tumor of the optic nerve in a child 3½ years of age, the histologic examination of which showed "endothelioma with some fibromatosis, no glial elements demonstrated." He referred to von Hippel's discussion of tumors of the optic nerve that show both "gliomatosis and fibromatosis" and stated that "such tumors have nothing to do with generalized neurofibromatosis."

Mayer (1937) stated: "As contributions to the literature on von Recklinghausen's disease have multiplied, no longer is multiple neurofibromatosis, a fibroblastic diathesis with early optic nerve involvement in neurofibromatosis, considered a rare disease." He reported the occur-

rence in a woman 43 years of age of a slight generalized pigmentation of the skin, a soft subcutaneous nodule behind the ear, a nodule adhering to a tendon of the finger, vision in one eye of 20/200 and in the other of 20/50 and marked concentric contraction of the visual fields. The histologic diagnosis based on biopsy of a nodule was neurofibroma. The father and paternal grandfather had progressive loss of vision, and the latter had a growth on a finger and contraction of the hand. The diagnosis of tumor of the optic nerve was apparently not verified by operation.

Wheeler (1936) reported the occurrence of a tumor of the right eyelid in a child which proved to be plexiform neurofibromatosis. The right eye was sightless. It had been trephined for a congenital buphthalmos when the child was but a few months old. The eye, with some attached orbital tissue, was finally enucleated. Pathologic examination by Dr. A. G. Reese showed that there was neurofibromatosis of the orbit, the choroid and the ciliary body and that the optic nerve was also involved. The sections of the optic nerve showed "neurofibromatosis and complete atrophy of the nerve fibers, with no medullation seen." [11]

Worster-Drought, Dickson and McMenemey (1937) presented an interesting study of multiple meningeal and perineural tumors, with analogous changes in the glia and ependyma, for which they suggested the term "neurofibroblastomatosis." They reported 2 cases which revealed a multiplicity of lesions, including subcutaneous neurofibromas, multiple lesions of the cranial nerves and meningeal tumors. The optic nerve in 1 case was surrounded by a meningeal tumor which extended to the eyeball. The tumor consisted of a moderately cellular growth arranged in definite whorl formation, though also palisading. Particles of brain sand were present. The authors, however, did not discuss tumors of the optic nerve with relation to Recklinghausen's disease, since the growth around the nerve was presumably an extension from a similar growth within the cranium and therefore was not considered primary. They remarked that the majority of meningeal tumors occur singly, but they cited 11 recorded cases in which they were multiple. They further stated: "In association with peripheral and central neurofibromata, they are, however, practically always multiple, only three cases in which they are single having been described."

Stern (1937) reported the occurrence of a tumor of the optic nerve, "a spongioblastoma—polare," in a girl of 3 years of age; according to the clinical history there were small café au lait patches scattered over

11. Dr. Reese permitted me to study some of the sections from this interesting case, but there was not sufficient tissue available for complete study of the intraorbital portion of the nerve.

the trunk and limbs. Curiously, the author made no comment on this finding. Papilledema was reported but no exophthalmos. Death followed an exploratory operation for suspected cerebellar tumor. Autopsy revealed a tumor of the right optic nerve, chiasm and thalamus.

Lisch (1937) reported 3 cases of Recklinghausen's disease with involvement of the eye. All of these patients showed nodules on the iris; in 2 cases this constituted the only ocular symptom. In the third case there was also a nevus of the bulbar conjunctiva and cornea and bilateral involvement of the optic nerve. Examination of the fundi showed choking of the optic disk with eventual atrophy. Roentgen examination showed a widening of both optic canals and a bulging of the sella turcica, indicating a tumor of the optic nerves and optic chiasm, which the author stated was probably a spongioblastoma. The patient, a man 44 years of age, had numerous cutaneous tumors and pigmented spots, which had begun to develop when he was 17 years of age. The failing vision had been noted only within a year prior to this study.

Aegerter and Smith (1937) reported diffuse generalized neurofibromatosis, associated with a central spongioblastoma of the hypothalamic area and a semineoplastic glial proliferation of the optic nerves and chiasm, in a child 2 years old. At autopsy the optic nerves were found to be much enlarged. Sections of the optic chiasm and nerves showed a homogeneous, uniform, diffuse overgrowth of adult fibrillary astrocytes, for which they suggested the term "astrocytosis." The sections of the optic nerve in this case revealed a structure almost identical with that in 1 of my cases. Exophthalmos was not mentioned in the case history, though primary atrophy of the optic nerve was recorded. Apparently the orbital portions of the nerves were not studied at autopsy. Had this child lived, it seems likely that further progress of the gliomatosis within the nerves in the orbit would have produced some degree of exophthalmos. This case history and study is one of great importance, particularly to ophthalmologists, because it reveals a type of lesion of the nerve and chiasm which may explain an obscure atrophy of the optic nerve associated with mild peripheral signs of Recklinghausen's disease in which exophthalmos may not be present. The mild nature of the peripheral lesions is significant. (Since this paragraph was written the tumor in case 4 of my series has been examined, and it also illustrates this point.) These authors offer the comment: "Speculation as to the nature of the process suggests some specific neuropathic growth-stimulating factor, which acts uniformly on the several component parts of the nervous system, especially on the various supportive cells including the glia, the endoneurium, the perineurium, and the epineurium."

Fuchs (1937) stated that he has seen 2 cases of Recklinghausen's disease with evidence of atrophy of the optic nerve, 1 of which he

reported. The patient, a man, was first seen in 1919. His vision had been gradually failing for four years. Both optic disks were pale. General examination showed two subcutaneous tumors of the Recklinghausen type. A diagnosis of neurofibromatosis (Recklinghausen) of the optic nerve was made. The patient was again seen twelve years later, when vision had diminished to perception of light. Numerous subcutaneous tumors had developed, confirming the previous diagnosis. No operation was performed, and the patient was living at the time of the report. Fuchs cited 2 other cases of involvement of the optic nerve in association with Recklinghausen's disease, namely, those of Wiegmann and Barber and Shaw.

Levitt (1937), reporting glioma of the chiasm and optic nerves in a woman of 43, remarked that primary tumors of the optic nerve are sometimes associated with generalized neurofibromatosis, or Recklinghausen's disease. He added that "no neurofibromatosis was found" in the case which he reported. He made the significant comment that many cases of unexplained blindness or atrophy of the optic nerve may be due to early tumors of the nerve, some of which have been incorrectly diagnosed as retrobulbar neuritis.

Busch and Christenson (1938) reported 2 cases of tumor of the optic nerves and chiasm. In the first the patient was a girl 7 years of age. None of the family had shown any similar tumor or any signs of Recklinghausen's disease. The patient herself had numerous pigmented spots and flat pigmented nevi but no cutaneous tumors. The chief symptoms were progressive failure of vision and headaches. Examination showed primary atrophy of the optic nerve, enlargement of the optic foramens and slight enlargement of the chiasmic sulcus. Tumors of both optic nerves, uniting in the chiasm, were found at operation. They seemed under considerable pressure. An incision was made in the tumor of the left optic nerve, through which tumor tissue bulged. A similar incision was made in the tumor on the right side. These tumors were then united by a transverse incision in the chiasm. The tumor tissue that bulged from this was removed and the incision widened. The patient made a good recovery, and vision was definitely improved. At the time of the report this improvement had been maintained for two and a half years.

In the second of these 2 cases the patient was also a girl of 7 years of age. Her mother and grandmother had typical Recklinghausen's disease. The patient showed pigmented areas but no tumors. There had been definite diminution of vision since she was 3 years old. Examination showed bilateral primary atrophy of the optic nerve. Roentgen examination revealed a marked enlargement of both optic foramens and considerable enlargement of the chiasmic sulcus. As in the first of these

cases, the tumor was partially removed at operation. Vision definitely improved after operation, and at the time the case was reported it had shown no change for the worse in the two years the child had been under observation.

Microscopic examination of the tumor tissues removed showed the growths in these 2 cases to be strikingly similar. The tumors closely resembled a spongioblastoma of the brain stem. "The most typical cell elements were the long cells 'oligodendrocytes or spongioblasts'; but the round cell type was also present; neuroglia fibers were present in association with the round cells." This type of glioma of the optic nerve should be distinguished from other gliomas of this region, the authors stated, since the clinical picture is so typical. In both these cases the peripheral signs were of the abortive type, which, according to the authors, are more apt to be associated with tumors of the optic nerve than the fully developed disease.

Stallard (1938) reported the occurrence of a tumor of the left optic disk and retina in a youth 19 years of age, whose left eye was removed for a supposed malignant neoplasm. The reports state that the tumor was composed of neurocytes and neurofibrils. Symptoms of a tumor of the brain developed, and the patient died after an exploratory operation. While no histologic examination of the intracranial lesion was made, the author is convinced that it was related to general neurofibromatosis, since the family history revealed that six members of two preceding generations showed evidence of multiple lesions, probably neurofibromatosis, with involvement of the optic and auditory nerves as well as the brain.

Schmidt (1938) reported the occurrence of subcutaneous nodules on the neck of a youth 16 years of age; these proved to be typical neurinomas. In addition, there were paralysis of the facial nerve, deafness on the left side, paralysis of the left leg and evidence of multiple neurinomas involving the central nervous system. Both optic disks were prominent, indicating involvement of the optic nerves near the globe, as the optic foramens were not enlarged. The author reported this as representing a rare form of Recklinghausen's disease with multiple lesions in the central nervous system.

Bailey and Herrmann (1938) reported extensive pathologic studies in 2 cases of multiple tumors of the nerves. In 1 of these cases there was no involvement of the optic nerves or of any of the structures of the eye. In the other case (1, B. S.) [12] multiple tumors of the peripheral nerves and failing vision were discovered. At the first examination the optic nerve heads appeared normal, but a diagnosis of generalized neurofibromatosis with glioma of the optic nerve and chiasm was made

12. This case was previously reported by Cushing (see page 988).

on the basis of the clinical findings. Later the optic disks showed a definite pallor, and symptoms of involvement of the auditory nerve and other cranial nerves developed. At autopsy it was found that the optic nerves "consisted mainly of a dense gliosis divided into funiculi by septums of connective tissue extending inward from the sheath. . . . The glial scar was composed of piloid astrocytes usually elongated in the long axis of the nerve, although there was a condensation of neuroglial fibrils often along the septums of connective tissue which ran at various angles to the main direction of the fibers of the gliosis." The tumor of the optic chiasm which extended into the hypothalamus was composed principally of large bipolar spongioblasts; a subcortical tumor of the cerebellum proved to be a protoplasmic astrocytoma; multiple areas of the abnormal neuroglial cells were also found in the brain and cerebellum.

In addition to the foregoing review concerning the relation of tumors of the optic nerve and Recklinghausen's disease, which is limited chiefly to the ophthalmologic literature, I have consulted a number of general articles concerning the latter disease. In 35 of these some visual defect is mentioned, and often atrophy of the optic nerve is reported, but no reference is made to tumors of the optic nerve or chiasm as a possible cause of the atrophy. A few case reports may serve to emphasize the fact that involvement of the optic nerve in this disease apparently has not been suspected.

Le Bell, in an article concerning Recklinghausen's neurofibromatosis in children, gives an excellent résumé of the disease with extended reference to the literature and a report of 3 cases, in 2 of which the patients were sisters. He failed to mention anything in connection with the eye, however, except in 1 case to comment briefly on the bilateral ptosis and its possible relation to plexiform neuromas of the eyelids. He did state, however, that the mother of these two children had multiple neurofibromatosis and an astrocytoma (presumably of the brain) and that she was totally blind before her death, which occurred at the age of 32. The history further relates that the mother's two sisters were also blind six and twelve months before their deaths. No specific comment is made concerning the importance of this ocular history. While this report may advance little argument in favor of the relation of tumors of the optic nerve to Recklinghausen's disease, it does indicate, by its absence of comment or data concerning the eyes in the recorded cases, that pediatricians are either unaware of such association or have not given it serious consideration.

Sharpe and Young (1937) presented a survey of Recklinghausen's neurofibromatosis, with a report of the clinical manifestations in 31 cases. They do not mention ocular changes in any of their case reports,

however, with one exception—case 30. The patient, a woman 33 years of age, gave a history of the enucleation of one eye at the age of 2 years because of a tumor (cutaneous tumors had developed at the age of 12).

In reviewing cases of Recklinghausen's disease observed in the department of medicine of the University of the Wisconsin General Hospital, 20 in number, some visual disturbance had been noted in 5 cases and atrophy of the optic nerve was described in 3. Owing to ignorance of the relation of the two conditions, detailed ophthalmologic studies were not made, nor was the presence of tumor of the optic nerve suspected. These do not include the 5 cases herein reported. Undoubtedly reports of numerous cases now on record have failed to reveal the real cause of the visual defects.

Comment.—The appended table lists the case reports of tumors of the optic nerve associated with Recklinghausen's disease which appear in the literature, including the 5 cases herein reported.[13] There are 37 authentic case reports, in most of which the diagnosis was confirmed at operation or at autopsy. In a few of the cases a clinical diagnosis of early tumor of the nerve seems justified on the basis of the recorded findings. No doubt in some of these in which exophthalmos was not present early "gliomatosis" of the nerve would be found.

Atrophy of the optic nerve was more frequently reported than choked disk, but no doubt choking of the disk may have preceded atrophy in some of the cases. Bilateral involvement of the nerve was reported in 15 cases, while in 16 there was some form of intracranial involvement. In 16 cases the peripheral signs were recorded as hereditary. Ages of the patients ranged from 2 years to 52 years. Twenty-two patients were females and 14 males. (In 1 case the sex was not recorded.)

The pathologic diagnosis of most of the tumors was some form of glioma, though 4 were classified as endotheliomas, 2 as neurofibromas and 2 as neurofibromatosis. The two latter terms, however, appear to have been used loosely and do not refer to actual histologic studies of the tumors.

A number of the cases cited in the review of the literature are not included in the table, since the evidence presented was not conclusive. No doubt numerous other cases are on record.

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13. Since this paper was completed I have studied 2 additional cases by permission of Dr. Rodman Irvine. One of these has been reported (Rand, C. W.; Irvine, R., and Reeves, D. L.: Primary Glioma of the Optic Nerve, Arch. Ophth. **21**:799 [May] 1939). In both of these cases the patients were young children. The lesions of the peripheral nerves consisted of numerous café au lait patches distributed over various parts of the body. In the case cited the clinical significance of the cutaneous lesions was not recognized and so was not reported.

The general physical examination in many recorded cases is too incomplete to venture any generalization concerning all of the tumors of the optic nerve reported in the literature. If one can judge by the increasing number of cases which have been reported in the past ten years in which the tumors have been associated with Recklinghausen's disease, there must have been a considerable number overlooked in the past. The condition even in those cases in which there are no demonstrable peripheral signs should be held under suspicion, for it may be related to this syndrome.

Since the tumors of the optic nerve, especially the gliomas, which are not associated with Recklinghausen's disease, are histologically identical with those which are found associated with it, Fleischer concluded that the two are homologous.

It may be that patients with Recklinghausen's disease with associated ocular changes, particularly tumors of the optic nerve, fail to reach the general physician, since most of these patients naturally consult the ophthalmologist. The general manifestations of the disease in these cases are frequently so mild that they have gone unnoted or have been considered of no importance by the family physician. The ophthalmologist's attention is fixed on the ocular lesion, and he may and often does overlook the associated changes in other parts of the body, since these may be insignificant. Thus the patient is operated on and is discharged without the true nature of the disease being recognized. The case reports cited in the bibliography to this paper, however, indicate that an increasing number of ophthalmologists appreciate the significance of this association.

A familial or hereditary history of patients affected with tumors of the optic nerve has not been revealed in reports by authors discussing them. The associated condition, Recklinghausen's disease, however, is usually hereditary.

Since patients with tumors of the optic nerve associated with Recklinghausen's disease frequently show only the mildest general manifestation of the disease, such as café au lait–pigmented spots in the skin, it is important that ophthalmologists subject every patient, especially children, to a rigid search for these patches. They should be on the alert also for other general signs, such as deformities of the skeleton, particularly scoliosis.

The association of tumors of the optic nerve with Recklinghausen's disease can no longer be regarded as a coincidence. From the evidence now available, it appears that tumors of the optic nerve, especially of the glial type, are in many instances but one manifestation of the disease. While they are more often associated with the abortive peripheral type of the disease, deep-seated lesions are likely to accompany them.

Data on Cases of Tumor of the Optic Nerve Associated with Recklinghausen's Disease

Case No.	Author	Year	Age, Sex	Pathologic Diagnosis	Autopsy	Operation	Associated Lesions of Peripheral Nerves	Unilateral	Bilateral	Family History of Recklinghausen's Disease	Comment; Associated Lesions of Central Nervous System
1	Michel.....	1873	16 M	Glioma of optic nerve and chiasm	Yes	No	Elephantiasis neuromatodes of leg	Yes	....	.....	
2	Westphalen.....	1887	35 F	No microscopic study	Yes	....	Multiple fibromas of skin	Yes	....	.....	Dural psammofibroma
3	Fehr.....	1913	27 M	Neurofibromatosis of optic nerve	....	Yes	Multiple neurofibromas	Yes	....	No family history	No definite tumors found at operation; possible early gliosis
4	Christin and Naville	1920	..	Neurofibroma	Yes	No	Neurofibromatosis, general	....	....	.....	Neoplastic nodules in brain pressing on optic nerve
5	Parker; Benedict	1922	17 M	Endothelioma	Yes	Yes	Neurofibromatosis of peripheral and central nervous systems	Yes	....	No family history	Meningiomas of brain and cord; multiple tumors of spinal cord
6	Steurer.....	1922	12 M	No pathologic study of optic nerve	Yes	....	Tumors of peripheral nerves; pigmented spots	Yes	....	.....	Multiple neuromas at base of brain; tumor of acoustic nerve
7	Martin and Cushing	1923	6 F	Glioma of nerve and chiasm	Yes	Yes	Mild abortive type; pigmented spots only	....	Yes	.....	
8	Martin and Cushing	1923	20 F	Glioma of nerve and chiasm	....	Yes	Tumors of peripheral nerves; spots, and fibromata molluscа	....	Yes	Yes; pigmented spots	
9	van der Hoeve	1925	37 F	Neurofibromatosis	....	Yes	Typical neurofibromatosis of peripheral nerves	....	Yes	.....	No histologic study of tumor
10	Holström.....	1928	4 F	.....	No	No	Abortive type; pigmented spots only	Yes	....	Father had spots	Exophthalmos; enlarged optic canals; clinical diagnosis only
11	Holström.....	1928	5 F	.....	No	No	Tumors of peripheral nerves and pigmented spots	Yes	....	Father and sister	Optic canals enlarged; slight exophthalmos; clinical diagnosis only
12	Schnyder.....	1928	21 M	Diffuse gliosis of optic nerve	Yes	....	Tumors of third and ninth intercostal nerves	....	Yes	.....	Glioma of infundibulum
13	Cushing.....	1930	12 F	Glioma of optic nerves and chiasm	....	Yes	Pigmented spots and tumors of peripheral nerves	....	Yes	Father had mild form	Also reported later by Bailey and Herrmann (see case 22)

14	Goldstein and Wexler	1932	52 F	Glioma of optic nerve; spongioblastoma	Yes	....	Multiple tumors of peripheral nerves, and spots	Yes	....	.....	No clinical symptoms; discovered at autopsy
15	Bueno and Liombart	1933	6 F	Glioma; oligodendrocytoma	Yes	Yes	Mild abortive type; pigmented spots only	Yes	....	.....	
16	Hartmann.....	1933	8 F	Polymorphous meningioblastoma	Yes	....	Pigmented spots and a few tumors of peripheral nerves	Yes	....	.....	
17	Hartmann.....	1933	27 F	Neurofibroma	Yes	....	Pigmented spots and tumors of peripheral nerves	Yes	....	.....	
18	Hartmann.....	1933	7 M	.....	No	No	Pigmented spots and tumors of peripheral nerves	Yes	....	.....	Enlarged optic foramens; clinical diagnosis—tumor of optic nerve
19	Foerster and Gagel	1934	11 M	Gliomatosis; proliferation of Schwann cells	Yes	....	Pigmented spots and tumors of peripheral nerves	....	Yes	No family history	Diffuse gliosis of central nervous system; chiasm involved
20	Fleischer.....	1934	3½ F	Gliomatosis of chiasm	Yes	....	Pigmented spots, tumors of peripheral and sympathetic nerves	Yes	....	Father	Gliomatosis of central nervous system
21	Fleischer.....	1934	Boy M	Gliomatosis (?)	No	No	.....	....	....	.....	Reports case similar to case 20; no details of history
22	Shapland and Greenfield	1935	22 F	Endothelioma (psammoma)	Yes	....	Multiple neurofibromas	Yes	....	.....	Meningioma of brain; glioma of frontal lobe and cord
23	Stern.....	1937	3 F	Glioma; spongioblastoma of chiasm	Yes	....	Pigmented spots only	....	....	.....	Lesion of thalamus
24	Aegerter and Smith	1937	2 F	Glioma; astrocytosis	Yes	....	Generalized (spots); neurofibromatosis	....	....	.....	Chiasm; thalamus also involved
25	Worster-Drought and others	1937	25 M	Meningioma (psammoma type)	Yes	....	One neurofibroma on back; no spots	Yes	....	.....	Central neurofibromatosis; meningioma; neuroma of acoustic nerve; astrocytoma of cord
26	Lisch (case 3)....	1937	44 M	?	No	No	Numerous spots and tumors of peripheral nerves	....	Yes	No family history	Bilateral choked disks; optic canals enlarged; clinical diagnosis
27	Fuchs.....	1937	37 M	.....	No	No	Pigmented spots; numerous tumors of peripheral nerves	....	Yes	.....	Bilateral atrophy of optic nerve; neurofibromatosis of optic nerves; clinical diagnosis

Data on Cases of Tumor of the Optic Nerve Associated with Recklinghausen's Disease—Continued

Case No.	Author	Year	Age, Sex	Pathologic Diagnosis	Autopsy	Operation	Associated Lesions of Peripheral Nerves	Unilateral	Bilateral	Family History of Recklinghausen's Disease	Comment: Associated Lesions of Central Nervous System
28	Mayer.....	1937	43 F	.....	....	....	Pigmentation of skin; neurofibromas of peripheral nerves	....	....	Father and grandfather	Biopsy showed tumor of peripheral nerves; neurofibroma; atrophy of optic nerve; clinical diagnosis, neurofibromatosis
29	Busch and Christenson	1938	7 F	Glioma; oligodendrocytoma	....	Yes	Pigmented spots only	....	Yes	.....	
30	Busch and Christenson	1938	7 F	Glioma; spongioblastoma	....	Yes	Pigmented spots only	....	Yes	Mother and grandmother	Chiasm also involved
31	Stallard.....	1938	19 M	Glioma of optic nerve head (neuroma)	....	Yes	.....	....	....	Many cases in family	Tumor of brain
32	Bailey and Herrmann	1938	12 F	Glioma; astrocytosis; spongioblastoma	Yes	Yes	Pigmented spots; fibromata molluscа; tumors of peripheral nerves	....	Yes	Father had general form	Numerous tumors of peripheral nerves and roots of spinal nerves; astrocytoma of brain
33	Schmidt.....	1938	16 M	.....	No	No	Subcutaneous nodules; neurinoma	....	Yes	.....	Multiple neurinomas of central nervous system; clinical diagnosis
34	Davis.....	1939	4 F	Glioma; astrocytoma	....	Yes	Café au lait spots	Yes	....	Mother and brother	Brother (case 35) also had similar glioma of optic nerve
35	Davis..... ...	1939	6 M	Glioma; astrocytoma	....	Yes	Café au lait spots; scoliosis	Yes	....	Mother and sister	Sister (case 34) also had similar glioma of optic nerve
36	Davis.....	1939	3 F	Gliomatosis; glioma; astrocytoma	Yes	Yes	Spots; plexiform neurofibromatosis of orbit and globe	....	Yes	Mother	Glioma of brain; gliomatosis of chiasm, medulla, pons, thalamus, etc.
37	Davis.....	1939	20 F	Glioma, cystic	....	Yes	Café au lait spots only	....	Yes	Grandfather	Glioma of chiasm, cystic
38	Davis.....	1939	27 F	Gliomatosis	....	Yes	Café au lait spots; small subcutaneous tumors	....	Yes	?	One child of patient has many pigmented spots on body

It is a curious clinical fact that tumors of the optic nerve do not usually accompany the more typical variety of Recklinghausen's disease in which there is widespread tumor formation all over the body, though there are notable exceptions to this. No satisfactory explanation for this is known.

The term "neurofibromatosis" or "neurofibroma," as applied to tumors of the optic nerve, should be abandoned, since it conveys the impression that the lesion resembles, or is identical with, neurofibromas of the peripheral nerves. It is my belief that they are an expression of the same general disease, but the histologic structure of the tumors is different. The tumor of the optic nerve is not a "neurofibromatosis" or "neurofibroma" but is usually a glioma or at times an endothelioma. It is possible that the finer branches of the peripheral or sympathetic nerves which enter the optic nerve stem with the blood vessels (Salzmann) along the pial invaginations might be subject to a neurofibromatosis in its strictest sense. The term has been frequently loosely employed, however, to describe the tumors which belong to the glial or endothelioma groups.

While it must be admitted, as von Hippel has pointed out, that proliferation of the arachnoid sheath, a structure presumably derived from the mesoblast, accompanies most of the gliomatous tumors of the optic nerve, this appears to be a secondary process which is induced by the glial proliferation of the nerve. Since, however, proliferation of the sheath of the nerve may occur independently, in the form of an endothelioma (meningioma), and this type of tumor accompanies Recklinghausen's disease at times, it must be admitted that this process may be an inherent part of the tumor growth and therefore may be dependent on the same stimulating growth factor or embryologic defect or whatever may be the underlying cause of the disease.

SUMMARY

This paper is a clinical and pathologic report of tumors of the optic nerve associated with Recklinghausen's disease, based on a study of 5 cases and a review of the literature.

So-called primary tumors of the optic nerve usually appear as one of two types, namely, gliomas and endotheliomas, the former being much the more common. Endotheliomas resemble those found in the brain, known as meningiomas or meningeal fibroblastomas. They arise from the dura or arachnoid sheath of the nerve or at times by extension from similar growths within the cranial cavity.

This study indicates that glial tumors start with an abnormal proliferation of the normal adult types of neuroglia of the nerve stem. After varying periods of growth, the abnormal neoplastic neuroglial

cells penetrate the pia, with the formation of a gliomatous tumor in the sheath. Proliferation of the mesothelial cells of the arachnoid follows the glial penetration of the pia, with the formation of a tumor-like mass in this portion of the nerve sheath. Later, intermingling of the proliferated cells from these two areas produces a complex histologic structure, the precise nature of which is difficult to interpret unless earlier stages of the growth have been studied.

Study of sections from these tumors reveals five different stages in the evolution of their growth, each of which is described.

Since these growths exhibit all the characteristics of true tumors, they should be designated as gliomas. Such terms as gliomatosis, astrocytosis, etc., should be used merely as descriptive terms for the earliest phase of their development. Complete histogenesis of the neoplastic cells has not been determined. Such types as spongioblastoma, spongioneuroblastoma, astrocytoma and oligodendrocytoma have been reported.

The outstanding feature of the neoplastic cells was excessive fiber formation within as well as without the nerve stem. This, together with the general character of the cells as revealed by special staining, indicates that predominant cell types were astrocytes, so that these tumors are designated astrocytomas.

The 5 cases herein reported were all associated with the abortive type of Recklinghausen's disease. Other lesions, such as plexiform neurofibromatosis of the orbit and globe, were present in 1 case, while manifestations of involvement of the central nervous system, such as gliosis of the chiasm and other areas of the brain, and a glioma of the temporal lobe of the brain were also encountered.

The review of the literature reveals at least 32 authentic cases of tumors of the optic nerve associated with Recklinghausen's disease. Many other cases of the latter disease, in which reduced vision and atrophy of the optic nerve were reported, probably fall within this classification. This association can no longer be disregarded or considered as merely coincidence.

The cause of Recklinghausen's disease and related lesions is not known. Pathologists are in disagreement concerning the nature of the tumors which accompany the disease. The lesions which make up this syndrome are more widespread than at first believed. One group of pathologists maintain that tumors of the peripheral nerves arise from some defect in the sheath of Schwann cells, a neuroectodermal derivative, while others assert that they arise from the fibrous elements of the nerves.

Studies of del Río Hortega, which are endorsed by Penfield, indicate that the oligodendroglia of the central nervous system, which includes the optic nerve, is homologous with the Schwann cells of the peripheral nervous system. A similar function of these two cell elements, namely,

maintenance of the myelin sheath of the nerve, is therefore probable. A defect of these homologous structures has been suggested, therefore, by del Río Hortega as a common source of origin of tumors of the optic nerve and tumors of the peripheral nerves.

Attempts to find some common background for all the tumors which make up the Recklinghausen syndrome, as now known, is complicated by the great dissimilarity in structure of some of the tumors. This suggests that the primary lesion in this complex disease must be sought in some degenerative change which primarily affects the nerve substance itself, while the tumors which follow may be secondary growths in the various supportive elements.

That tumors of the optic nerve probably belong to a system disease, as originally suggested by Emanuel, is borne out by the simultaneous appearance of multiple lesions in the central and the peripheral nervous system, by the fact that the tumors are bilateral at times and, further, by the fact that multiple involvement of the nerve has been reported. The slow rate of growth and the relatively benign nature of the tumors are characteristic of other lesions associated with this syndrome.

This study and review of the literature have led me to conclude that tumors of the optic nerve are in many if not most instances but a part of a more widely disseminated lesion of the peripheral and central nervous systems, commonly referred to as neurofibromatosis or Recklinghausen's disease.

The term "neurofibromatosis" or "neurofibroma" as applied to tumors of the optic nerve should be abandoned, for they are usually gliomas or endotheliomas.

Figure 1 is a drawing of sections of the tumor shown in figures 58 and 59.

The staff of the department of photography of the University of Wisconsin Medical School prepared the photographs and photomicrographs published in connection with this presentation. Miss Angela Swenson, technician in ocular pathology, prepared the numerous specimens required in this study. Dr. E. L. Goar and Dr. W. L. Benedict permitted me to examine and to report on specimens of tumors in their collections.

Dr. Percival Bailey on two occasions examined and discussed with me a number of my slides, and Dr. Frederick Verhoeff also examined and commented on specimens. I do not wish to imply, however, that these men are responsible for or are in accord with the conclusions I have drawn.

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ABSTRACT OF DISCUSSION

DR. PERCIVAL BAILEY, Chicago: Dr. Davis has made a most careful and useful study of these tumors, and his conclusions seem to be perfectly logical. These gliomatous tumors may involve the optic nerves in either their extracranial or their intracranial portion or both. In either case they may be associated with manifestations of Recklinghausen's disease elsewhere in the body. In 1930, in collaboration with Fulton, I published such an example of an intracranial glioma of the optic nerve (*Arch. argent. de neurol.* **5**: 1-27, 1930). The patient, a girl of 6 years, had numerous pigmented areas in the skin over the buttocks.

When these gliomas occur intracranially they are usually composed of spindle-shaped cells (Bailey, P., and Eisenhardt, L.: *J. Comp. Neurol.* **56**: 391-430, 1932). Even Lundberg admits this but followed del Río Hortega in maintaining that the neoplastic cells are of oligodendroglial origin. Russell and Bland believe them to be astrocytic. However it may be with the intracranial gliomas, Dr. Davis has shown that those which develop in the intraorbital portion of the optic nerves are mainly astrocytic with a variable admixture of oligodendroglial cells.

His demonstration of the glial nature of the proliferation in the pia-arachnoid is important. Oberling has long maintained, on the basis of such extensions of glial tissue into the leptomeninges over the brain as well as over the optic nerves, that the leptomeninges are of neuroectodermal origin; he has thereby caused great confusion in the terminology of intracranial tumors. It seems to me that Dr. Davis has settled the problem so far as the orbital tumors are concerned. The glial proliferation in the leptomeninges is of optic origin, and the arachnoidal proliferation is secondary.

The operative approach which he has used is logical and safe and effectively answers Dandy's dogmatic disapproval of an ophthalmic approach to these tumors. No one who knows how little can be accomplished by intracranial operation could be enthusiastic about the transfrontal route. In spite of the rarity of these cases, Dr. Davis has rightly called the attention of ophthalmologists to the association of these tumors with other manifestations of Recklinghausen's disease, a lesson which might profit all physicians, especially neurologists and neurosurgeons.

DR. JESSE M. LEVITT, Brooklyn: The main thesis of the presentation has been a correlation of tumors of the optic nerve with neurofibromatosis, or Recklinghausen's disease. Dr. Davis has shown that about 10 per cent of the cases of tumor of the optic nerve reported in the literature (which includes the 5 cases in the present paper) were associated with neurofibromatosis of the peripheral nerves. This percentage was posibly considerably higher, considering that the lesions of Recklinghausen's disease may have been overlooked or disregarded and the fact that 60 to 75 per cent of the cases of tumor of the optic nerve occur in the first decade of life while the manifestations of neurofibromatosis of the peripheral nerves usually become evident at puberty and in many cases later in life.

It is not impossible that in the future primary tumors of the optic nerve occurring without any other abnormality will be considered the sole or initial manifestation of Recklinghausen's disease, but for the present the tendency to link them as part of this syndrome gives an entirely new outlook for future clinical study.

I wish to report briefly 3 cases illustrating the three different clinical types of tumors of the optic nerve: (1) intracranial (2) intraorbital and (3) intraocular.

The first case (Tumor of the Optic Chiasm and Optic Nerves, ARCH. OPHTH. **18**: 91 [July] 1937) was that of a 43 year old white woman who had progressively lost vision in the left eye over the course of many years until it was completely blind and who had a painless proptosis and ptosis of the same eye of recent origin. The left eye also presented divergence, limitation of motility downward and nasally, a dilated pupil that reacted consensually but not directly to light and complete primary atrophy of the optic nerve. The right eye had a corrected vision of 20/20 and was normal in every respect, except that study of the visual field disclosed a temporal hemiachromatopsia for red and green, indicating chiasmal involvement. General physical examination and laboratory studies gave negative results; there was no neurofibromatosis. Roentgenograms showed a markedly enlarged left optic foramen, erosion of the left sphenoid ridge and a shallow sella turcica with erosion of the anterior and posterior clinoid processes. Craniotomy was performed, and a massive chiasmal growth was exposed. Removal was not attempted. The patient died on the twelfth postoperative day, and postmortem examination showed a striking picture: The left optic nerve was about the size of a lead pencil and was discolored, cystic and neoplastic in appearance. The optic chiasm was replaced by a mass of brown and yellow neoplastic tissue with small cystic areas. The left optic nerve, where it passed through the optic foramen, had eroded the surrounding bone, resulting in a friable and crumbling sphenoid ridge, and

passing into the orbit, it mushroomed out into a red fleshy growth which occupied the retrobulbar space. The right optic nerve was enlarged to about twice the normal size, and at its proximal portion it was infiltrated with neoplastic tissue spreading from the chiasm. There appeared to be a thinning of the third ventricle due to pressure upward of the chiasmal mass. Microscopic examination revealed a glioma of a vascular nature.

The second case, reported by permission of Dr. I. D. Kruskal, of Brooklyn, is that of a 9 year old white girl who had become entirely blind in the right eye in the course of a year and a half and whose parents reported progressive proptosis of the same eye over the course of a half year. The right eye presented on examination partial ptosis, proptosis of 8 mm., a semidilated fixed pupil, a pale optic disk with an elevation of 8 diopters and congested retinal veins with many superficial flame-shaped retinal hemorrhages. The left eye was normal in every respect. General examination gave negative results; there was no neurofibromatosis. Roentgenograms disclosed a generalized haze in the left orbit, interpreted as infiltration of soft tissue, and normal optic foramens and skull. A course of radiation therapy was without beneficial result. A Krönlein operation was performed, and a mass the size of a hazelnut, filling the apex of the orbit and surrounding the optic nerve, was exposed and removed.

Dr. Bernard Samuels reported the growth to be a glioma of the optic nerve, probably an astrocytoma, and Dr. Verhoeff classified it as a coarsely reticulated type of glioma. Eight months later the globe had receded to a normal position but was markedly divergent; the disk was completely atrophic, and the fundus showed widespread chorioretinitis. Fourteen months after the Krönlein operation was performed the globe was straightened by resection of the internal rectus muscle and severance of the adhesions of the external rectus muscle to the wall of the orbit. The child was not seen again until four and a half years after the removal of the orbital tumor, when she was admitted to the neurologic service in a state of semicoma with a history of intermittent attacks of headache, vomiting and loss of consciousness during the two months prior to admission. Both eyes were exophthalmic. The right pupil was maximally dilated and did not react; the left was slightly dilated and reacted sluggishly. The region of the right disk was occupied by a whitish irregular ovoid mass, which probably was a gliomatous replacement of the optic nerve, and the left disk was atrophic. The child died before a clinical investigation could be carried out, and permission for autopsy was not obtained. Death was considered to be the result of extension of the glioma into the chiasm and hypothalamus with resultant obstruction of the third ventricle.

The third case is one of suspected neoplasm of the optic nerve head. The patient has been under the observation of Dr. M. J. Buonaguro, of Brooklyn, who gave me the privilege of making an examination and of presenting this most unusual case. The patient, a 46 year old white man, first examined in October 1934, has in the left eye an immobile solid-appearing mass projecting into the vitreous in front of, and completely obscuring, the optic disk. The surface of the mass is smooth and pinkish, owing to fine innumerable blood vessels. It is capped by an irregularly crescentic zone of blood red hue. Pressure on the globe

blanches the surface, and on release of pressure the color becomes deep orange and then pinkish yellow. There are several small discrete white spots in the fundus temporally.

With the exception of slight displacement of the retinal vessels emerging from the nasal side of the disk zone, the vessels appear normal. The eye is outwardly normal. There is no proptosis. The tension is normal. The peripheral field of vision is full, and the blind-spot is markedly enlarged and almost reaches the fixation zone. The optic foramen is of normal size. The Wassermann reaction of the blood is negative. The vision of the eye is 20/200 with correction and has not altered during the four and a half years of observation. There has been a slight increase in the size of the mass and an appreciable increase in the number of white spots in the fundus. A cataract was removed by the intracapsular method from the other eye in May 1938, and the fundus is entirely normal. It is largely speculative as to the type of lesion that is present, but owing to the obvious vascularity it is felt that the tumor may be of vascular origin.

Dr. F. Park Lewis, Buffalo: It may be worth while to mention briefly a case of this kind because of the fact brought out by Dr. Davis that it is of such infrequent occurrence. He reported 300 cases. I have no doubt that if cases that have come under the observation of individual physicians were also reported one would find they are much more common than is believed.

A case of this character came under my observation two years ago. There was marked proptosis in the right eye and atrophy of the optic nerve, which had been gradualy progressing under the observation of an optometrist for five or six years. The proptosis measured about 4 mm.; there were no evidences of Recklinghausen's disease. The case was particularly interesting as a case of Recklinghausen's disease was available for study at the same time and comparison of the two was easily made. There was no involvement anywhere except the tumor found in the optic nerve. It was removed intraorbitally without removal of the eyeball by my associate Dr. Hague, but later the eyeball became so irritable that it became necessary to remove it. Since that time there has been no irritation whaever, and that is about a year ago. There are no evidences anywhere else of Recklinghausen's disease. The left eye is normal in every particular, and the diagnosis on the basis of microscopic examination at the United States Museum was a definite glioma.

The case is reported to add 1 more case without complication to those already reported.

Dr. Alan C. Woods, Baltimore: My reason for discussing the paper is to protest most earnestly against a statement made by Dr. Bailey, that orbital tumors should be approached by the frontal route. It is my privilege to work in a hospital with a large neurosurgical service, where many orbital tumors are studied. In many instances these tumors have been removed elsewhere by the frontal route, and the patients are seen first with orbital recurrences or evidences of intracranial extension. Other patients have not been operated on. It was formerly my habit to approach orbital tumors by the frontal, or Krönlein, route, and I had my share of recurrences and later evidences of intracranial extension.

After several such disastrous experiences by operation through the frontal route, it is now almost a routine procedure with me to refer all deep orbital tumors to the neurosurgical service for operation by the transfrontal route, a bone flap being turned down from above and the roof of the orbit opened. In the hands of a competent surgeon, this is a procedure with little more, if as much, danger as the frontal, or Krönlein, approach. It permits the removal not only of the orbital portion of the tumor but of any intracranial extension.

Too frequently the ophthalmologist going in from in front merely cleans out the orbital portion of the tumor and leaves his patient to die from cerebral metastases or extension. Therefore, I should like earnestly to protest against Dr. Bailey's frank advocacy of the frontal route.

DR. FREDERICK A. DAVIS, Madison, Wis.: I wish to thank the gentlemen who have discussed the paper for their very generous criticisms. I am especially grateful to Dr. Percival Bailey and feel highly honored that he was kind enough to come to this Section to discuss my paper.

With regard to the lesion of the disk mentioned by Dr. Levitt, I have referred in my paper to 2 growths of this nature, 1 of which was a true glioma of the retina. It was reported by McLean, and so far as I know is the only true glioma of the retina on record.

As to Dr. Wood's remarks, it is interesting that the brain surgeon should endorse my method of approach while the ophthalmologist favors the brain surgeon's approach.

In 2 of the cases reported the transfrontal procedure was used, since the chiasm was involved. If the chiasm is involved it is useless to try to eradicate the growth, because it is hopelessly inoperable. The best that one can do is to decompress the optic nerve by removing the roof of the optic foramen and make an incision in the sheath of the nerve, which was done in 1 case. Since gliomas grow extremely slowly, some slight vision may be preserved for a considerable period of time by this procedure.

I believe that these tumors of the optic nerve, as I have tried to point out, are merely one manifestation of a generalized disease. They are a part of a system disease. Therefore, other lesions presumably may exist in the chiasm, the brain (as was shown in one case here reported) and perhaps in the fellow optic nerve. So, after all, operation on the tumor of the orbit is nothing more than a palliative procedure to relieve exophthalmos and to preserve the globe. I do not believe that the glioma of the optic nerve necessarily extends back into the cranial cavity. That, of course, is possible, but in following the history of most of these cases and reading the autopsy reports, it will be found that other separate foci may already exist in the brain. Further, lesions of the central as well as of the peripheral nervous system in Recklinghausen's disease are usually multiple.

INDUCED SIZE EFFECT WITH THE EYES IN ASYMMETRIC CONVERGENCE

KENNETH N. OGLE, PH.D.
HANOVER, N. H.

When the eyes are turned in order to observe an object to the right or to the left of the median plane at near vision, the images of that object in the two eyes may be different in size because the distance from one eye is greater than that from the other eye. The smaller image would be expected in the eye that turns nasally, since the object is farther from that eye.

The results of a number of different experiments,[1] however, provide evidence that some type of change in the relative sizes of the ocular images may occur when the eyes are turned in asymmetric convergence; this change offsets, or tends to offset, the difference in the sizes of the retinal images which would exist because of the difference in the distance of the object from the two eyes.

This apparent change was investigated for visual distances of from 5 meters, where none could be measured, to 20 cm., where a large change was measured. The phenomenon was found principally in the vertical meridian, though for certain observers it occurred also in the horizontal meridian in some experiments. It has been pointed out, however,[1b] that the evidence for such a compensation for the difference in the sizes of the images is not entirely conclusive, because different results were found, depending on whether or not movements of the eyes were involved in the experimental comparison of the sizes of the images. That is, in most of the experiments in which the comparison of the sizes of the images was made from contours seen peripherally, with steady central fixation, the changes in the sizes of the images were found to be much less. In view of these results, other types of experimental means should be brought to bear on the problem.

From the Division of Research in Physiological Optics, the Dartmouth Eye Institute, Dartmouth Medical School.

1. (*a*) Herzau, W., and Ogle, K. N.: Ueber den Grössenunterschied der Bilder beider Augen bei asymmetrischer Konvergenz und seine Bedeutung für das zweiäugige Sehen (Ein Beitrag zur "Aniseikonia"-Forschung), Arch. f. Ophth. **137**:327-363, 1937. (*b*) Ogle, K. N.: Relative Sizes of the Ocular Images of the Two Eyes in Asymmetric Convergence, Arch. Ophth. **22**:1046 (Dec.) 1939.

It is believed that the phenomenon which has been described as the induced size effect [2] provides such a means and that it is an entirely different approach to the problem.

Briefly, the induced effect can be described as follows: Under ordinary circumstances, when a vertical difference is introduced in the sizes of the images of the eyes by placing before one eye a meridional size lens with magnification properties only in the vertical meridian all objects in the binocular visual field immediately appear displaced from their original positions somewhat in the sense of a rotation about a vertical axis in the median plane. The effect is especially evident if the field is relatively free from perspective clues. A surface parallel to the frontal plane at the fixation point actually appears nearer on the side of the eye whose image is larger in the vertical meridian and farther away on the side of the eye having the smaller image. This apparent rotation of the binocular field, caused by a difference in the sizes of the images in the vertical meridian, constitutes a new phenomenon in binocular vision. It cannot be accounted for on any known functional or geometric basis, for, according to the evidence accumulated in the literature, stereoscopic depth perception cannot arise from a vertical disparity of retinal images.

This effect is to be distinguished from a similar, though simpler phenomenon, in which an apparent rotation displacement of objects in the binocular field occurs when a meridional size lens, which magnifies only in the horizontal meridian, is placed before one eye.[2a] In that case, the false space rotations (which are in the direction opposite to those of the induced effect) can be attributed directly to changes in the horizontal disparities of the retinal images in the meridian of stereoscopic depth perception. These changes associated with a difference in the size of the images in the horizontal meridian take place in accordance with geometric optics and are susceptible to mathematical analysis.[3] Hence this phenomenon has been designated a geometric effect, in contrast to the induced size effect in which no such geometric interpretation is possible.

Returning now to the induced effect, experiment has shown that when a series of meridional size lenses of increasing magnification in the vertical meridian are introduced before one eye, the corresponding

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2. Ogle, K. N.: (*a*) Induced Size Effect: I. A New Phenomenon in Binocular Space Perception Associated with the Relative Sizes of the Images of the Two Eyes, Arch. Ophth. **20**:604-623 (Oct.) 1938; (*b*) II. An Experimental Study of the Phenomenon with Restricted Fusion Stimuli, ibid. **21**:604-625 (April) 1939; (*c*) III. A Study of the Phenomenon as Influenced by Horizontal Disparity of the Fusion Contours, ibid. **22**:613-635 (Oct.) 1939.

3. For example, see Ogle, K. N.: Die mathematische Analyse des Längshoropters, Arch. f. d. ges. Physiol. **239**:748-766, 1938.

apparent rotations of a test plane increase up to a maximum, beyond which with further increases in the difference in the sizes of the images in the vertical meridian a decrease in the apparent rotation occurs. Figure 1 is the graphic illustration of a set of data showing the typical sigmoid curve. These data represent the angles through which an observer rotated a test surface about a vertical axis, from the frontal parallel plane, in order for the surface to appear "frontal" for each of a sequence of differences in the sizes of images in the vertical meridian which were introduced by the meridional size lenses.

The average difference in the sizes of the images in the vertical meridian at which the maximum apparent rotation occurs, as well as

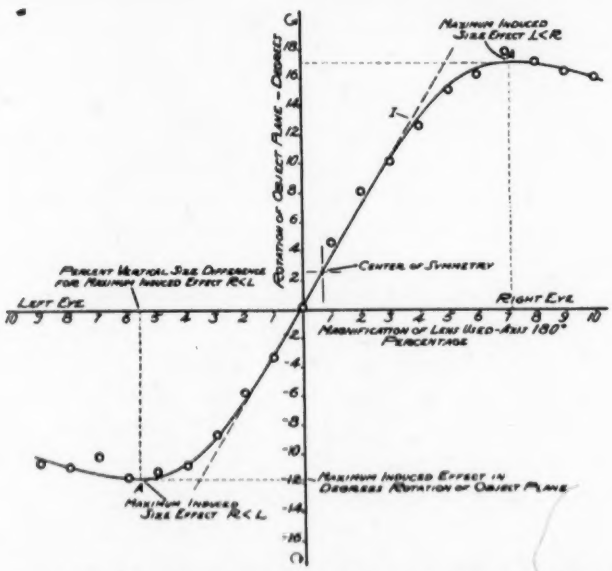
Maximum Induced Size Effect L<R
Center of Symmetry
Left Eye
Right Eye
Magnification of Lens Used-Axis 180°
Percentage
Maximum Induced Effect in Degrees Rotation of Object Plane
Maximum Induced Size Effect R<L

Fig. 1.—Graphic representation of typical data showing the induced size effect. Data of R. H. D. for a visual distance of 40 cm.

the magnitudes of the maximum rotations themselves, is fairly constant for each observer, provided the surface pattern is not changed. The study of the various experimental results suggests that the phenomenon of the induced effect arises from some type of physiologic process and that it has a connection with the fusion or interpretation effort associated with retinal images of unequal vertical disparity. The curve itself represents an amplitude (for given experimental conditions) within the limits of which the effect occurs. Experiment has shown that irrespective of the particular pattern on the test plane, the curve is symmetric in shape and the point of symmetry is relatively stable for each observer. It is believed that the repeatability and universality of the effect make it a means by which phenomena dealing with the relative sizes

of the ocular images of the two eyes can be studied. This paper describes experiments in which the S curve (as the sigmoid curve of the effect will be called) is used to study the relative sizes of these images when the eyes are turned into a position of asymmetric convergence. This study was but one phase of the various aspects of the work on the induced size effect.[4]

METHOD

The difference in the sizes of the retinal images that might be expected when the eyes are in asymmetric convergence, due to the difference of the distance of the object from the two eyes, may be considered an overall difference. This would be especially true if the face of the object observed would be normal (or nearly so) to the line joining the interpupillary midpoint and the fixation point on the object.

When a given difference in the sizes of the images is introduced between the eyes when they are in symmetric convergence and the data for the complete induced size effect S curve are obtained, the resultant curve should be displaced from the curve taken without such a difference. The nature of this displacement will be clear from the following facts: An overall size lens can be considered a combination of two equal meridional size lenses whose principal meridians are oriented at axis 90 and axis 180 degrees respectively. The apparent rotation of the test plane caused by the lens whose axis is 180 degrees will be due to the induced effect, while that of the lens whose axis is 90 degrees will be due to the geometric effect. Since the S curve itself is a phenomenon of difference in the sizes of the images in the vertical meridian, it is clear that a constant difference will be additive to the differences used to obtain the curve, and thus the origin of the curve should be displaced along the horizontal axis of the graph. For example, if a meridional size lens whose axis is 180 degrees is kept before the right eye and then the data are obtained for the complete S curve, that curve will be displaced theoretically to the left by the amount of the given difference in the sizes of the images in the vertical meridian (fig. 2). The magnitude of the maximum rotations should remain the same; only the differences in the sizes of the images in the vertical meridian at

4. After the data for this study had been completed (summer 1938), a paper was published by G. Schubert (Zur "Aniseikonie"-Frage, Arch. f. Ophth. **140**:55-60, 1939) which denied the general conclusions based on the previous measurements of the relative sizes of the ocular images with the two eyes in asymmetric convergence (footnotes 1 *a* and 1 *b*). Schubert attempted to explain those measurements on a special involvement of the receptor and motor apparatus of the two eyes. The results of the present study, which bring new evidence to confirm the previous investigations, may have a bearing on his conclusions. This general problem will be considered at another time.

which these maxima occur should be displaced. An analogy to this displacement might be the shift of the objective limits of the range of accommodation of an eye when a spherical power lens is placed before it.

In a similar manner the S curve should be displaced along the vertical axis of the graph when a given difference in the sizes of the images in the horizontal meridian is introduced. For example, a given difference introduced by a meridional size lens with an axis of 90 degrees before the right eye should cause the S curve to be displaced downward (fig. 3). In this case the differences in the sizes of the images in the vertical meridian at which the maximum rotations occur are not influenced; but the initial rotation of the test plane due to the geometric effect of the lens becomes additive to the rotations caused by the induced effect.

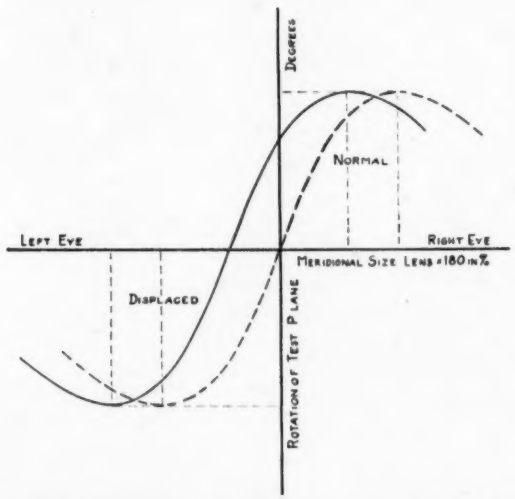

Fig. 2.—Graph illustrating the displacement of the induced size effect S curve from the normal curve when a meridional size lens which increases the size of the image of the right eye only in the vertical meridian is kept before the eye throughout the experiment.

The change in the normal S curve, due to a given overall size lens before one eye, will be a combination of these displacements, depending on the relative sensitivity of the eyes to the two effects. With the simple pattern used in the experiments described here, the sensitivity of the induced effect is generally about one-half as great as that of the geometric effect, and therefore a vertical displacement might be expected. With the overall size lens there should always be a displacement of the curve horizontally, because of the vertical component of the overall magnification which will displace the differences in the sizes of the images at which the maximum rotations occur.

When the eyes are used in an asymmetric convergence position at near vision, a constant difference in the sizes of the images is introduced by the difference in the distance of the test plane from the two eyes. Hence, a displacement would be expected of the S curve taken with the eyes in this position from the curve taken in symmetric convergence. The determination of these displacements is the purpose of the present experiments. It is important, however, to study experimentally the displacements of the S curve caused by an overall difference in the sizes of images with the eyes in symmetric convergence. Whether the induced effect S curve is a suitable means for investigating the relative sizes of the ocular images would depend on the results.

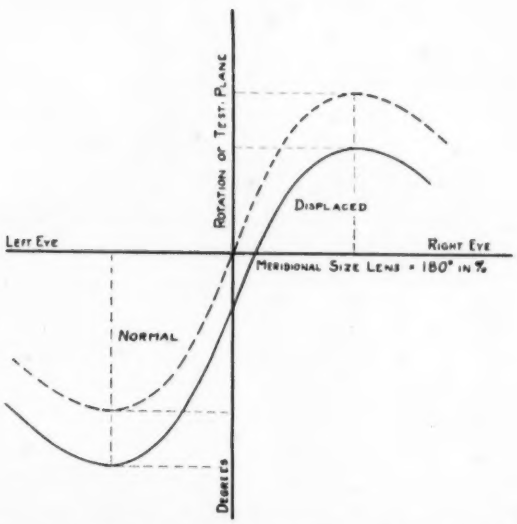

Fig. 3.—Graph illustrating the displacement of the induced size effect S curve from the normal curve when a meridional size lens which increases the size of the image of the right eye only in the horizontal meridian is kept before the eye throughout the experiment.

APPARATUS AND PROCEDURE

The apparatus used is illustrated schematically in figure 4. The head of an observer is held in position by a wax bite and suitable forehead rests. Through a slit in a screen, which excludes empiric factors as far as possible, the observer fixates a vertical surface, designated as the object plane, or test plane, at a visual distance of 40 cm. The object plane consists of a sheet of plate glass supported in a frame which can be rotated about a vertical axis in the plane of the surface. By means of a cord, the plane can be rotated by the observer. Contours for the fusion pattern are drawn on the surface of the glass with india ink or black paint. A large sheet of cardboard, uniformly illuminated, is suspended behind the object plane for a background, against which the contours are seen by the observer.

The object plane, background and other parts of the apparatus are mounted as a unit on a tongue which can be turned about a vertical axis that passes through the midpoint of the centers of rotation of the eyes. By turning this tongue sideways, the plane will be in such a position that the eyes will be in asymmetric convergence when they are looking directly at it. Suitable lens holders (not indicated in figure 4) are so mounted before the eyes that their axes coincide with the visual axes of the eyes in all positions of asymmetric convergence. A protractor scale, with a suitable indicator below the frame of the test plane, shows the angular position of the plane as measured from a position at right angles to the center line of the tongue.

The simple fusion pattern on the object plane [2b] was made up as follows: In the center of the plane, a horizontal row of small dots, irregularly spaced, was drawn to provide the stereoscopic stimuli by which the observer could ascertain the rotational position of the plane. A vertical black thread to control the convergence of the eyes was stretched through the center of the plane. Above and

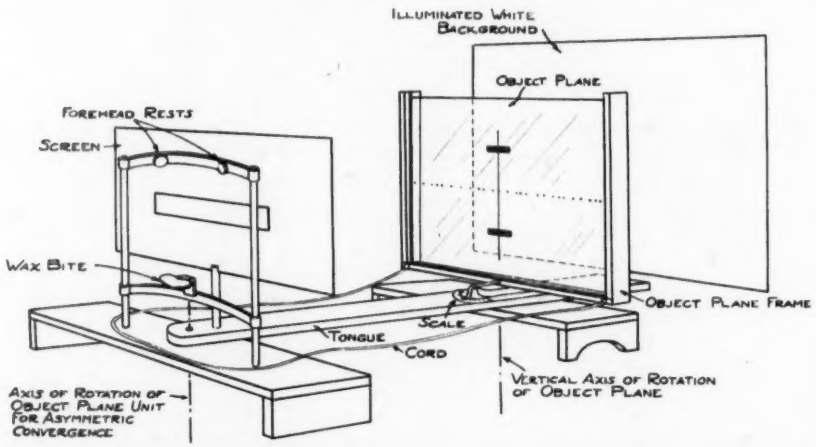

Fig. 4.—Schematic drawing of the apparatus used for studying the induced size effect of the eyes in asymmetric convergence.

below the center of the plane, at a distance of 3.5 cm., small black rectangles, 1.5 by 0.15 cm., were drawn in a horizontal position (fig. 4). These rectangles provided the necessary restricted fusion contours in the vertical meridian, without which the induced effect does not occur when a difference is introduced in the sizes of the images of the eyes in the vertical meridian.[2b] A modification of this fusion pattern is the substitution of small black hemispheres for the rectangles. The former have the advantage that they do not change shape when the plane is rotated.

In making a setting of the object plane, the observer is instructed to adjust its rotational position so that it appears "normal," that is, at right angles to the subjective direction of the central point of the test plane.[5] For symmetric convergence, this amounts to setting the plane for an apparent frontal position. In asymmetric

5. The observer was often told to think of the object plane as a mirror and to rotate it to such a position that he would be looking directly at his image in the center of the plane.

convergence, it is merely a "normal" setting. Objectively, the true normal position would correspond to a zero scale reading on this apparatus. For the purposes of this experiment, however, the particular criterion used in the setting of the plane is not so important as long as it is the same for all the adjustments in each set of data. A different criterion for each set would result merely in a displacement along the vertical axis of the graph. The same criterion, however, should be used throughout the series of data.

The procedure followed in determining the data for the S curve was for the observer to make a number of independent settings of the plane for each of a sequence of meridional size lenses placed at axis 180 degrees before one eye. Lenses up to and including 12.5 per cent were used. The corresponding rotational positions of the test plane were recorded by an assistant. The averages of the settings for the various lenses are then plotted as shown in figure 1,[2] in which the per cent magnification of the lenses is plotted on the abscissa and the corresponding degrees of rotation of the test plane are plotted on the ordinate.[6]

TABLE 1.—*Typical Data of the Induced Effect When a 3 Per Cent Overall Size Lens is Kept Before the Right Eye or the Left During the Experiment* *

Magnification of Meridional Size Lens at Axis 180°, %		Normal	3% Overall Size Lens Before Right Eye	3% Overall Size Lens Before Left Eye
Lenses before right eye	12.5	16.1 (1.0)	4.1 (0.1)	22.2 (0.7)
	10.3	15.5 (1.0)	8.7 (0.6)	22.4 (1.0)
	8.2	15.4 (0.3)	7.8 (0.6)	23.2 (0.4)
	6.0	14.5 (1.0)	10.1 (0.3)	18.6 (0.6)
	4.0	12.9 (0.5)	6.5 (1.1)	16.7 (0.5)
	2.0	8.0 (0.5)	5.3 (0.2)	11.4 (0.3)
	None	2.5 (0.3)	0.4 (1.4)	7.7 (0.8)
Lenses before left eye	2.0	—2.4 (0.4)	—6.8 (0.5)	1.1 (0.2)
	4.0	—4.4 (0.5)	—11.9 (0.4)	2.2 (0.3)
	6.0	—6.2 (1.2)	—14.4 (0.1)	0.3 (0.3)
	8.2	—6.8 (0.1)	—17.2 (1.1)	2.2 (1.2)
	10.3	—7.5 (0.5)	—16.5 (0.7)	0.6 (0.6)
	12.5	—5.8 (0.4)	—17.7 (1.2)	1.5 (0.4)

* The data (of R. H. D.) are the degrees of rotation of an object plane (with mean deviations) about a vertical axis, measured from the normal position (the rotation in which the right side of the test plane moves away from the observer is taken as positive). The plane is adjusted by the observer for an apparent normal position for each of a sequence of meridional size lenses which introduce increasing differences in the sizes of the images in the vertical meridian. The visual distance was 40 cm.

RESULTS

Overall Size Lenses.—Since the induced and geometric effects are opposite in direction, when a constant overall difference in the sizes of the images of the two eyes is introduced there may be little effect on the initial adjustment of the plane if the fusion contour pattern on the test plane is complex. For the aforementioned reasons some vertical

6. Calculation shows that the rotation of the test plane from the normal position in asymmetric convergence bears nearly a linear relation to the corresponding equivalent differences in the sizes of the images in the horizontal meridian (geometric effect) between the two eyes for angles of the order of 20 degrees. Hence, variations in the shape of the S curves found in asymmetric convergence cannot be ascribed to asymmetries in the rotational positions of the test plane.

displacement of the S curve from the normal curve would be expected to result from an overall size lens. For the purposes of these experiments, the exact influence of an overall size difference on binocular space perception is not necessary. The important thing is to find whether any horizontal displacement of the induced effect S curve occurs in response to the vertical component of the magnification of the overall size lens.

The typical data obtained by one observer are given in table 1. These show the degrees of apparent rotation of the object plane caused by each of a sequence of meridional size lenses placed (axis 180 degrees) before one eye and then the other—first, for the normal eyes, and then when a 3 per cent overall size lens is placed before the right eye

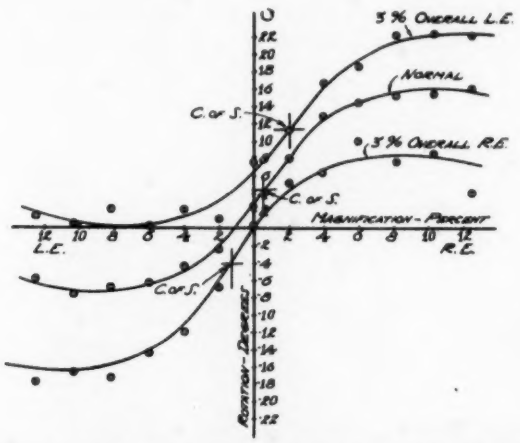

Fig. 5.—Graphic illustration of the induced effect data obtained by R. H. D. when a 3 per cent overall size lens was placed before the right eye and then the left.

and then the left. The data are illustrated graphically in figure 5. Similar results of other observers are shown in figures 6 and 7, overall size lenses of 3 and 5 per cent respectively being used.

An inspection of these graphs shows that a regular displacement of the curves occurs when an overall size lens is kept before one eye throughout the experiment. When the overall lens is before the right eye, the center of symmetry of the curve is displaced to the left of that of the normal curve; when the lens is kept before the left eye, the displacement is to the right. These displacements are in the directions that might be anticipated, though the magnitudes are generally less than those that might be expected. At present this discrepancy in the magnitudes of the displacements cannot be accounted for, except perhaps on a hypothetic basis. Its existence, however, is of less importance

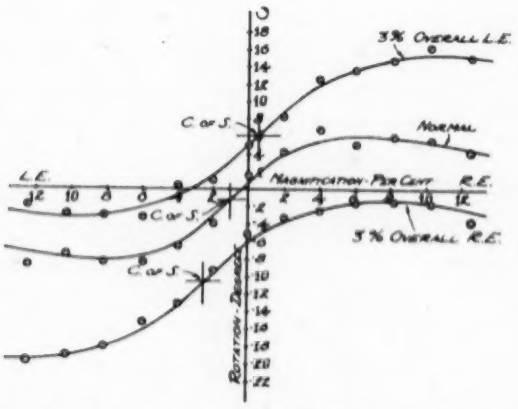

Fig. 6.—Induced size effect curves obtained by G. S. N. when a 3 per cent overall size lens was placed before the right eye and then the left.

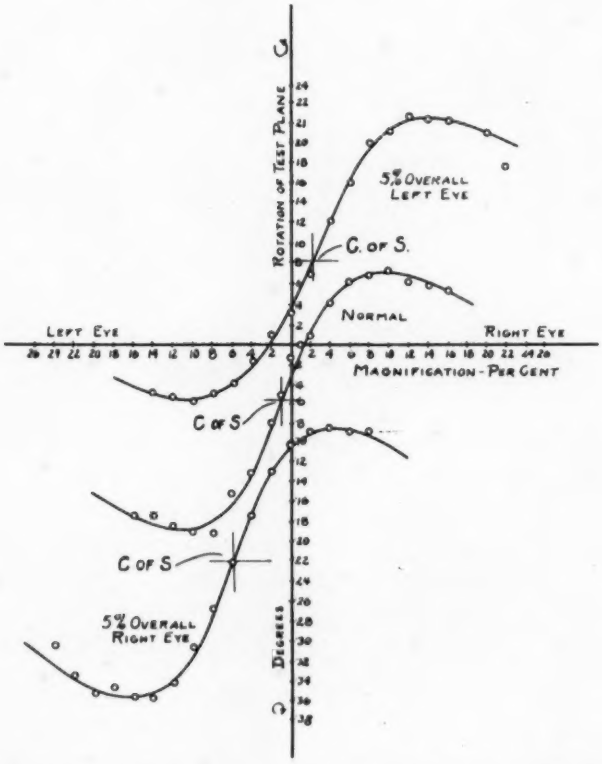

Fig. 7.—Induced size effect curves obtained by K.N.O. when a 5 per cent overall size lens was placed before the right eye and then the left.

than the truly appreciable horizontal displacement of the S curves that actually does occur. Also to be noted are the anticipated vertical displacements of the curves, due to the fact that with the simple test pattern used the sensitivity of the induced size effect is less than that of the geometric effect.

Asymmetric Convergence.—When an object is observed in asymmetric convergence, the distance from each of the two eyes is different, and this should result in an initial difference in the sizes of the retinal images. The induced size effect S curves, then, should be displaced from the curve obtained in symmetric convergence, unless some type of compensatory change has occurred in the relative sizes of the ocular

TABLE 2.—*Data Obtained by G. S. N. for the Induced Size Effect in Symmetric Convergence and in Asymmetric Convergences of 10 and 20 Degrees to the Right and to the Left for a Visual Distance of 40 cm.**

Meridional Size Lenses		20° Left	10° Left	Symmetric Convergence	10° Right	20° Right
Lenses axis 180° before right eye	12%	+14.4 (0.7)	+11.9 (0.4)	+13.5 (0.3)	+ 8.9 (0.5)	+ 8.6 (0.6)
	10%	+15.7 (0.3)	+12.5 (0.1)	+12.8 (0.2)	+10.9 (0.2)	+10.0 (0.4)
	8%	+15.7 (0.5)	+12.2 (0.8)	+13.6 (0.5)	+10.3 (0.6)	+10.3 (0.1)
	6%	+13.4 (0.3)	+11.6 (0.3)	+12.4 (0.7)	+ 8.8 (0.2)	+10.3 (0.2)
	4%	+ 9.3 (0.3)	+10.1 (0.7)	+ 9.6 (0.9)	+ 5.7 (0.2)	+ 7.3 (0.7)
	2%	+ 5.6 (0.4)	+ 5.8 (0.6)	+ 4.8 (0.2)	+ 3.4 (0.7)	+ 3.4 (0.8)
	None	+ 1.4 (0.3)	+ 0.3 (0.2)	− 0.3 (0.1)	− 2.4 (0.3)	− 2.1 (0.2)
Lenses axis 180° before left eye	2%	− 4.7 (0.2)	− 4.9 (0.4)	− 4.8 (0.3)	− 7.9 (0.1)	− 6.8 (0.4)
	4%	− 8.3 (0.4)	− 8.6 (0.4)	−10.7 (0.2)	−10.2 (0.1)	−11.9 (1.2)
	6%	−10.6 (0.3)	−10.9 (0.4)	−13.7 (0.4)	−12.9 (0.3)	−14.7 (0.4)
	8%	−13.3 (1.0)	−11.4 (0.6)	−13.6 (0.4)	−14.3 (0.7)	−15.8 (0.4)
	10%	−12.9 (0.7)	−11.6 (0.6)	−13.3 (0.6)	−13.3 (1.5)	−14.6 (0.4)
	12%	−11.0 (0.7)	−11.2 (1.6)	−11.9 (0.5)	−13.0 (0.7)	−12.6 (0.3)

* The data are the mean degrees of rotation of an object plane (with mean deviations) about a vertical axis from the normal position (counterclockwise rotations are taken positive) when the plane is adjusted by the observer for an apparent normal position for each of a sequence of meridional size lenses which introduce increasing differences in the sizes of the images in the vertical meridian.

images when the eyes are turned into positions of asymmetric convergence.

In table 2 the data of one observer are given for a visual distance of 40 cm. and for asymmetric convergences of 10 and 20 degrees to the right and to the left of the median plane. These data and those of two other observers are illustrated graphically in figures 8, 9 and 10.

At the visual distance of 40 cm. and for an average interpupillary distance (65 mm.), the difference in the relative sizes of the retinal images for an asymmetric convergence of 10 degrees would be about 2.8 per cent, and for 20 degrees it would be about 5.6 per cent.[1b] Hence, a measurable horizontal displacement of the S curve from that taken in symmetric convergence would be expected. For example, when the eyes are turned in asymmetric convergence to the right, a larger image in the right eye would be expected, and the S curve should be displaced

to the left relative to the curve obtained in symmetric convergence. In view of the experiments with the overall lenses, appreciable displacements would certainly be anticipated. The curve in each graph indicated by the broken line is the expected position of the induced effect curve according to the full geometric difference in the sizes of the retinal images due to the difference in the distance of the object plane from the two eyes.

Inspection of the actual S curves themselves shows that no regular displacement of this kind is evident. In fact, the curves present excellent

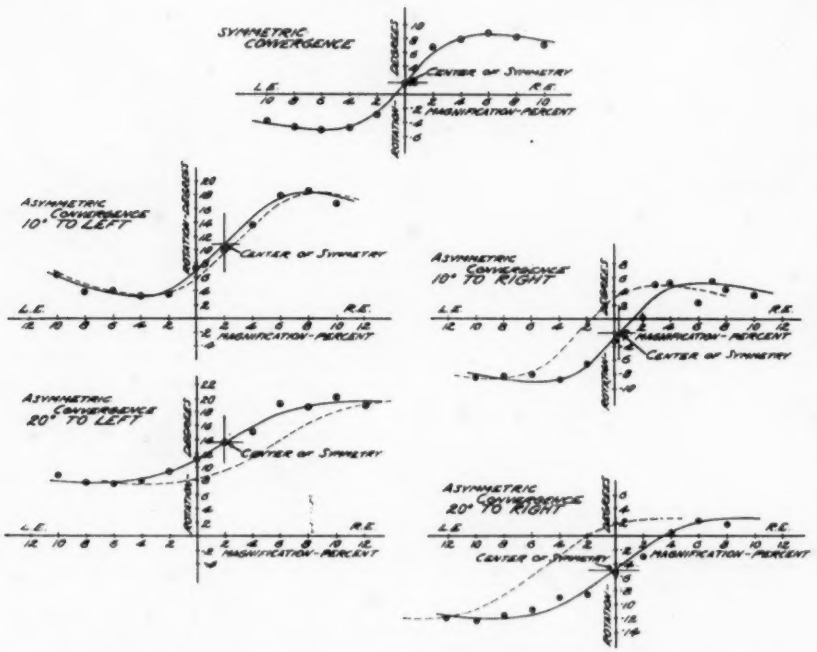

Fig. 8.—Induced size effect S curves found by R. H. D. with the eyes in symmetric and in asymmetric convergence. The visual distance was 40 cm.

evidence that no regular displacement occurs. Even the somewhat irregular displacements of several of the curves are far below the anticipated displacements (except perhaps for observer R. H. D. in looking 10 degrees to the left).

For a better quantitative comparison, the positions of the centers of symmetry for each curve, which are easily obtained by graphic means, are shown in table 3. The horizontal positions of the center of symmetry of the curves, that is, the vertical magnitude of the difference in the sizes of the images for the point of symmetry, are given in the first row of the table. The other derived data included in the table are for

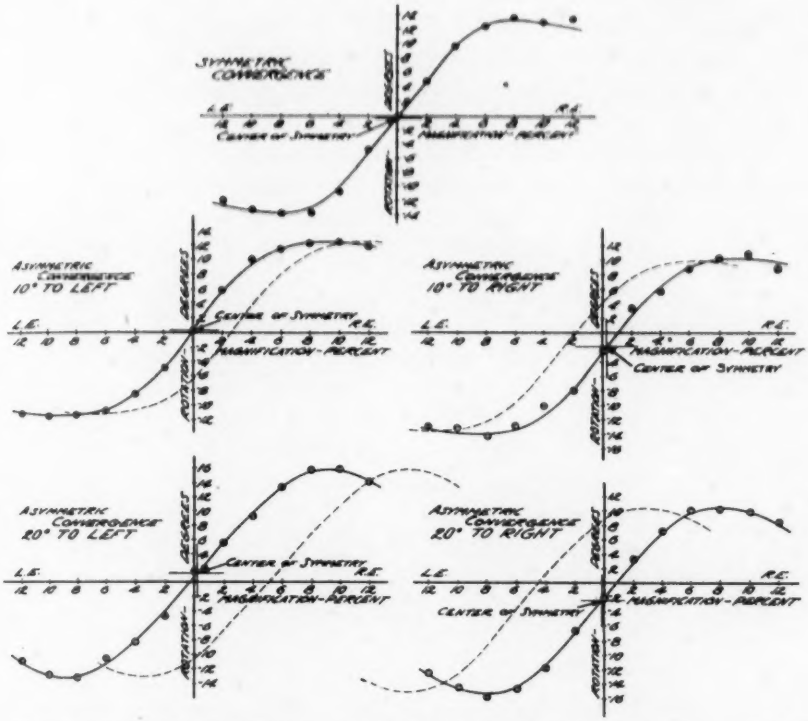

Fig. 9.—Induced size effect S curves found by G. S. N. with the eyes in symmetric and in asymmetric convergence. The visual distance was 40 cm.

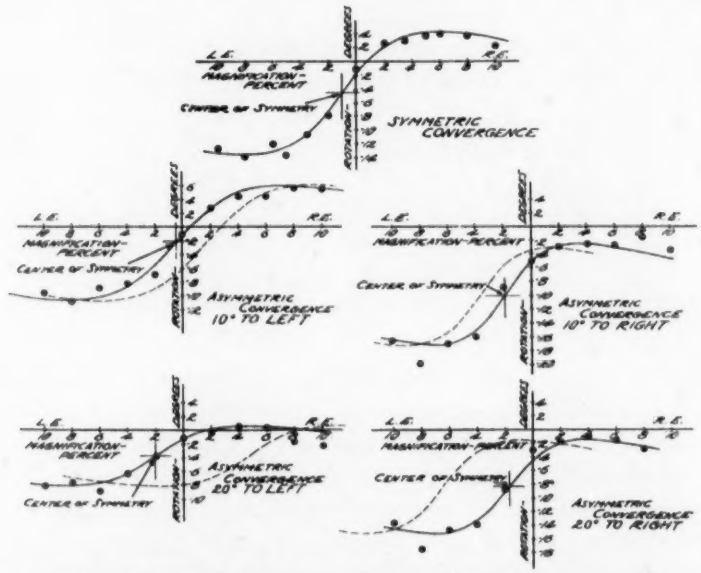

Fig. 10.—Induced size effect S curves found by K. N. O. with the eyes in symmetric and in asymmetric convergence. The visual distance was 40 cm.

general information as to the regularity of the curves in other respects. In general, inspection will show that for the same observer the various values pertaining to a given aspect are relatively constant, except for the displacement of the center of symmetry along the vertical axis of the graph.

TABLE 3.—*Summary of Important Values Derived from the Induced Size Effect S Curves for a Study of the Sizes of Ocular Images with the Eyes in Asymmetric Convergence*

Visual Distance of 40 Cm.		Asymmetric Convergence to Left		Symmetric Convergence	Asymmetric Convergence to Right	
		20°	10°		10°	20°
Observer K. N. O.						
Center of symmetry of S curves	Image size difference	R 0.6%	R 2.0%	R 1.0%	R 1.9%	R 1.8%
	Rotational position	−3.8°	−2.0°	−4.4°	−10.0°	−8.1°
Maximum induced size effect	Average image size difference*	6.5%	6.0%	6.5%	5.0%	5.5%
	Average rotation	4.4°	7.4°	8.7°	7.3°	6.6°
Sensitivity of induced effect		1.4°/%	2.5°/%	2.7°/%	2.9°/%	2.5°/%
Observer R. H. D.						
Center of symmetry of S curves	Image size difference	L 2.0%	L 2.2%	0.0%	L 0.4%	0.0%
	Rotational position	+13.5°	+10.6°	+1.8°	−1.8°	−5.0°
Maximum induced size effect	Average image size difference*	10.0%	8.0%	6.0%	6.5%	8.0%
	Average rotation	5.9°	7.6°	7.0°	6.9°	6.5°
Sensitivity of induced effect		1.2°/%	1.9°/%	2.3°/%	2.1°/%	1.6°/%
Observer G. S. N.†						
Center of symmetry of S curves	Image size difference	L 0.3%	0.0%	0.0%	L 0.3%	R 0.5%
	Rotational position	+1.8°	+0.4°	−0.3°	−1.8°	−2.4°
Maximum induced size effect	Average image size difference*	11.5%	9.0%	8.5%	9.0%	10.0%
	Average rotation	14.5°	12.1°	13.7°	12.0°	13.1°
Sensitivity of induced effect		2.5°/%	2.7°/%	2.6°/%	2.7°/%	2.9°/%

* Estimated to nearest 0.5 per cent.

† These data were obtained with a pattern on the object plane consisting of a ring of scattered dots instead of the rectangular contours. The center of the ring subtends approximately a visual angle of 5 degrees.

These last displacements raise the question whether any information is obtainable from these experiments regarding the relative sizes of the ocular images in the horizontal meridian. Answers to that question depend on what constitutes the criterion used for setting a plane subjectively in asymmetric convergence. Consider, for example, figure 11, in which the eyes are shown schematically in symmetric convergence and in asymmetric convergence of β degrees to the right. In symmetric convergence a frontal plane which is perpendicular to the median plane at

the fixation point is also tangent to the Vieth-Müller horopter circle. Tangency to the Vieth-Müller circle is the condition in which no difference exists in the sizes of the ocular images of the two eyes. If the plane is rotated about a vertical axis at the fixation point, the change in the disparities of the retinal images of points on the plane near the fixation point is the same as though all the disparities of a frontal plane in the horizontal meridian were increased by a constant amount.

In asymmetric convergence, the tangent to the Vieth-Müller circle is much inclined, being rotated from the frontal position by nearly twice the angle of the asymmetric convergence. Thus, if a plane is to have the same "pattern" of retinal image disparities as has the frontal plane in symmetric convergence, it must be placed at this inclination. The "normal" plane, which is at right angles to the line joining the fixation point and the interpupillary midpoint, has a pattern of retinal image

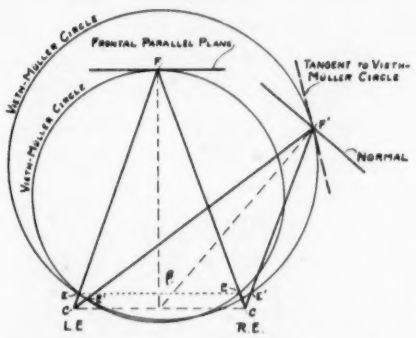

Fig. 11.—Diagram showing the positions of certain planes in symmetric and in asymmetric convergence which have importance in considering the relative sizes of the ocular images in the horizontal meridian.

disparities which differs from that of the frontal plane in symmetric convergence by a difference in the sizes of the images which corresponds nearly with that necessary to compensate for the difference in the distances of the plane from the two eyes.

The question of the criterion, then, arises in this manner: If the subjective pattern of retinal image disparities for the apparent normal plane in asymmetric convergence is the same as the pattern for the apparent frontal (normal) plane in symmetric convergence, then compensation for the difference in the sizes of the ocular images must occur when the eyes are turned asymmetrically, in the sense that the size of the image of the eye turned nasally becomes larger. If, on the other hand, the particular subjective pattern of retinal image disparities which corresponds to the normal position for each particular asymmetric convergence is different, then no compensation can be assumed. Of course, the change in these subjective patterns of retinal image disparities for the

same visual distance is equivalent to a difference in the sizes of the images in the horizontal meridian. Until something is known about the nature of the subjective criterion, no direct information regarding the relative sizes of the ocular images in the horizontal meridian is available from the results of these experiments.

It is of importance, however, to note in the graphs the consistent behavior of the vertical displacements of the curves for all three observers. When the eyes turn to the right, the centers of symmetry move downward; when they turn to the left, the centers move upward. The magnitude of the displacement is different for each of the three observers. This movement would indicate that the plane is adjusted in the direction of a rotation toward the tangent to the Vieth-Müller circle.

CONCLUSIONS

No regular horizontal displacement in the induced effect S curves occurs when the eyes are turned in asymmetric convergence, in spite of the geometric difference introduced in the relative sizes of the retinal images of the two eyes. Thus, one must assume that either there is a compensatory change in the relative sizes of the ocular images of the two eyes in the vertical meridian which offsets the geometric image difference or the conclusions regarding the influence of overall size lenses on the induced size effect S curve are invalid for the asymmetric convergence positions of the two eyes. Even the latter possibility would indicate some type of compensatory process to overcome the difference in the sizes of the images. In view of the other experiments [1] dealing with the relative sizes of the images of the two eyes in asymmetric convergence, it is believed that these experiments, making use of the induced size effect as a new means, give additional evidence to support the theory that a change in the relative functional sizes of the ocular images of the two eyes occurs in the vertical meridian when the eyes are turned in asymmetric convergence and that in general this change is of an amount which offsets the difference in the distance of the observed object from the two eyes.

No direct evidence as to a compensation for the difference in the sizes of the images in the horizontal meridian is available from these experiments.

TREATMENT OF VERNAL CATARRH WITH SOLID CARBON DIOXIDE

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The use of solid carbon dioxide in medicine is not new. This preparation was first employed by dermatologists for the removal of moles, warts, small epitheliomas, angiomas and nevi and for the treatment of xanthelasma, molluscum contagiosum and some diseases of the mouth and uterus.

Later its use was extended to the treatment of diseases of the eye, such as follicular conjunctivitis, lymphatic hypertrophy of the fornices, trachoma and vernal catarrh, but it never became popular, not on account of the results, which were found to be fairly satisfactory by all authors, but principally because the applications required a tedious preparation of the solid carbon dioxide from a tank containing the gas. Lately, as the commercial use of solid carbon dioxide has been extended for freezing purposes, it can easily be found in any candy shop; in the New York area it is distributed under the name of dry ice.

Ten patients were treated with solid carbon dioxide, and some were followed for more than four years to check up on possible relapses.

METHOD OF USE

From the cake of solid carbon dioxide a pencil can be made that can be held with a forceps, but on account of its friability it melts too soon under the pressure of the forceps.

To eliminate this disadvantage I devised a small container, consisting of a metal cylinder covered with wood, which acts as an insulator (fig. 1).

The end of the cylinder is left uncovered, to be applied directly over the vegetations.

Small pieces of solid carbon dioxide put into the container bring the temperature of the metal point to — 80 C., which is the melting point of solid carbon dioxide.

When the metal point is pressed over the conjunctiva for a few seconds, a bleached spot appears at the point touched, showing that the conjunctiva has been frozen in that area. By increasing the duration and the amount of pressure, the conjunctiva is frozen to a greater depth. By keeping the point of the container in contact with the conjunctiva, a layer of ice is formed by the tears, and the container sticks to the conjunctiva, interfering with the application. This disadvantage can easily be eliminated by cleaning the point with alcohol before each application, the freezing point of the alcohol being much lower than that of the tears.

The application is performed in the following manner:

Topic anesthesia is obtained with repeated instillation of a 4 per cent solution of cocaine hydrochloride for ten minutes. The lid is everted, and the cobblestone vegetations are clearly evident, care having been taken to protect the cornea with the everted lid. The container, prepared as described, is held with one hand, and the point is brought in contact with the vegetations and kept there for about forty seconds, moderate pressure being exerted. When the container is removed, it leaves a circular area of frozen tissue, which is white and solid. The point is cleaned with a swab steeped in alcohol, and the applications are repeated until the entire surface is covered. The conjunctiva is allowed to defreeze before it is replaced, to avoid injury of the tissue and contact of the frozen area with the corneal epithelium.

The usual reaction is that of congestion of the conjunctiva and slight pain, lasting about twenty-four hours.

The applications are repeated at weekly intervals.

Fig. 1.—Container for solid carbon dioxide, consisting of a metal cylinder covered with wood.

In some of the cases in which this form of therapy was used it was necessary to treat the condition for three years, though each year the conjunctiva improved appreciably. However, in a few cases the treatment was completed in five months.

Generally, the symptoms abate after the first few applications.

During the entire period of treatment any previous remedies were discontinued.

Four of the 10 cases here reported are from the Brooklyn Eye and Ear Hospital, 4 from the New York Eye and Ear Hospital and 2 from my private practice.

REPORT OF CASES

Case 1.—P. D. C., a man aged 25, of Italian extraction, entered the clinic of the Brooklyn Eye and Ear Hospital on March 21, 1935. He stated that his ocular condition had been present for two years and that the usual remedies given at different times in the clinics and by private physicians had been without benefit.

Examination showed a normal corneal limbus, a congested bulbar conjunctiva, lacrimation and a mucinous discharge, that was found later to contain eosinophils.

The tarsal conjunctiva of the eyes was covered with granulations of different sizes, arranged as a cobblestone pavement; the larger ones occupied the nasal part of the tarsal conjunctiva near the margin of the lid. Small red dots were seen on the larger granulations.

The patient was treated with solid carbon dioxide at weekly intervals, with improvement after the first few treatments. Gradually the granulations disappeared, leaving soft scars like those of a cicatricial trachoma. The patient has been examined from time to time until May 1939. On no occasion has he complained since 1936.

CASE 2.—J. R., aged 9 years, of Italian extraction, came to the clinic of the Brooklyn Eye and Ear Hospital on May 4, 1933. A diagnosis of vernal catarrh was made. As the usual remedies did not bring about any improvement, treatment with solid carbon dioxide was advised. The patient completely recovered after two years of applications.

CASE 3.—W. M., aged 8 years, of Jewish extraction, was seen at the Brooklyn Eye and Ear Hospital in August 1933. Solid carbon dioxide was used for a few weeks, with marked improvement, but the patient failed to come later, complaining that the treatment was too painful.

CASE 4.—A child aged 7 years, of Jewish-Polish extraction, was seen at the Brooklyn Eye and Ear Hospital in April 1933. Solid carbon dioxide brought about marked improvement in a few weeks, but the child failed to return because of pain from the treatments.

CASE 5.—P. C., a woman aged 32, of Italian extraction, was seen in my office on April 19, 1937. Her condition was of two years' duration. Solid carbon dioxide was used, and the patient completely recovered by November of the same year. She has been seen occasionally for refraction, and no recurrence of the vegetations has been noticed.

CASE 6.—T. L., aged 21, of Jewish extraction, came to the clinic of the New York Eye and Ear Infirmary on Sept. 8, 1936, where a diagnosis of vernal catarrh was made. The condition was treated for some time with usual remedies, with no apparent results. On April 3, 1937, treatment with solid carbon dioxide was begun and has been continued, as the patient has suffered a relapse of the condition in a milder form every spring.

CASE 7.—M. E., a man aged 28, of Jewish extraction, came to the clinic of the New York Eye and Ear Infirmary on Sept. 29, 1936. He was treated with solid carbon dioxide for a year and showed marked improvement, namely, the complete disappearance of the granulations. However, since he still complained of a burning sensation, he was referred to the allergy clinic, where he was found to be sensitive to a few allergens. After special care, he was reported to be improved.

CASE 8.—S. C., a man aged 29, of Jewish extraction, registered at the clinic of the New York Eye and Ear Infirmary on April 12, 1938, with a history of vernal catarrh of eight years' duration, with exacerbations from April to September.

In 1934 the condition was treated in some New York hospital; the conjunctiva of the upper tarsus in the left eye was removed, and a transplant of the mucous membrane from the mouth was done, with apparently no improvement, as new granulation formed near the transplant and some on the graft.

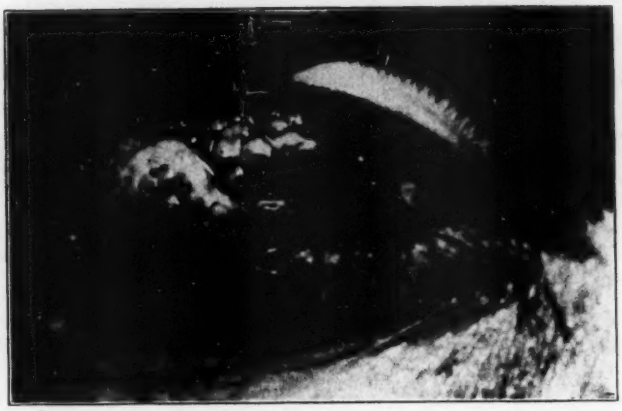

Fig. 2 (case 8).—Condition of the tarsal conjunctiva in April 1938.

Fig. 3 (case 8).—Condition of the tarsal conjunctiva in May 1939.

Fig. 4 (case 8).—Appearance of the right eye after treatment with solid carbon dioxide and of the left eye after transplantation of mucous membrane.

Later the patient was seen at the Roosevelt Hospital, where he received a complete examination in the allergy clinic and the rhinolaryngologic department. Cultures of material from the eye made at the Roosevelt Hospital showed Staphylococcus albus, indifferent streptococci and Streptococcus viridans. The patient was treated there for some time with a staphylococcus toxoid, autogenous vaccine and sulfanilamide. All therapy was without apparent benefit.

The examination in the clinic of the New York Eye and Ear Infirmary showed that the tarsal conjunctiva of the right eye was covered with large granulations disposed in a cobblestone fashion, mostly in the outer part of the lid and covered with a film of mucous discharge.

The right eye was treated weekly with solid carbon dioxide, with quick improvement. The symptoms subsided after the first application, and granulations disappeared completely toward the end of the year, seven months after the beginning of the treatment.

Figures 2 and 3 show the condition of the right eye before and after treatment. Figure 4 shows both eyes for comparison—the right eye, treated with solid carbon dioxide, and the left eye, in which, though transplantation of mucous membrane was done, there were a few vegetations of vernal catarrh near the margin of the lid.

CASE 9.—G. P., a man aged 27, of Jewish extraction, was admitted to the clinic of the New York Eye and Ear Infirmary on Aug. 17, 1938. The right eye only was affected with vernal catarrh of the tarsal type. Treatment with solid carbon dioxide was instituted in the usual manner up to November 1938, when the patient showed so much improvement that he was discharged. He was seen in June 1939, when he stated that he had had no further complaints.

CASE 10.—L. M., a boy 8 years of age, of Italian extraction, was seen in my office on May 13, 1939. The parents stated that he had suffered from redness and itching of both eyes for the last three years, in the spring. Examination showed congestion of the conjunctivas of both eyes, with gelatinous nodules at the limbus but no tarsal vegetations. The discharge was examined later and showed some eosinophils.

The same treatment as for the tarsal type of vernal catarrh was adopted, and the improvement was quicker and more remarkable. After only six treatments, the nodules disappeared from the limbus.

COMMENT

Solid carbon dioxide has a beneficial effect on the vegetations of vernal catarrh because of its freezing, and not because of its chemical, properties.

The temperature reached by the carbon dioxide when passing from a solid to a gaseous state is 80 C. below zero. In freezing the tissue, the carbon dioxide causes thrombosis of the small vessels of the vegetations, and consequently necrosis of the cells. New connective tissue is formed where the vegetations have been, and whitish shiny scars can be seen in the healed conjunctivas.

The generally recognized failure of any kind of treatment for vernal catarrh (such as application of radium, allergic desensitization, administration of vaccines or drugs or use of transplants of mucous mem-

branes) is probably due to the fact that the pathologic process of vernal catarrh lies not in the conjunctiva alone but deeper, in the superficial layers of the tarsus. That is probably why in some transplants the vegetations, after some time, reappear through the graft. With cauterization with solid carbon dioxide as suggested, namely, by exerting some pressure so that the freezing affects the superficial layers of the tarsus, the success of the treatment is considerably greater than with other known procedures.

The patients who respond to this type of therapy are those with the greatest hypertrophic changes. This leads me to believe that many conditions diagnosed as vernal catarrh are not true vernal catarrh but allergic conjunctivitis, with seasonal recurrence and no pathologic features of the vernal catarrh.

I cannot agree, then, with the author who recently made a classification of the different forms of vernal catarrh. In 1938 Whalman[1] stated that there are three forms of vernal catarrh, namely: (1) a simple one, "in which the conjunctiva is slightly thickened and pale and the entire palpebral surface is involved"; (2) a follicular form, with "all the characteristics of the simple form and, in addition . . . numerous small, round, discrete nodules," and (3) a vegetative form, in which "the conjunctiva has the appearance of a greatly thickened, warty mass."

During the discussion which followed Dr. Whalman's article, Dr. M. N. Beigelman agreed with him that the cobblestone granulations from the tarsal conjunctiva are characteristic of the advanced, final stage of vernal catarrh.

I cannot agree with either one of them on this subject, because if one were to follow a patient with the first or second forms of vernal catarrh for months or years, one would never see these small round nodules acquire the characteristics of the cobblestone granulations classically described in the textbooks.

Naturally the changes in the conjunctiva affected with typical vernal catarrh do not form in a few days, but the fact is that when the patients are first seen the "cobblestones" are already formed.

Moreover, the alterations of the "mild forms" disappear in some seasons, with the relief of the symptoms. The cobblestone vegetations last for years, though in some seasons they do not annoy the patient at all.

The fact that some patients with vernal catarrh have allergic reactions may be a coincidence and in no wise proves that the relation between allergy and vernal catarrh is that of cause over effect. On the

1. Whalman, H. F.: Vernal Conjunctivitis, Arch. Ophth. **20**:877 (Nov.) 1938.

contrary, the unsatisfactory results of therapeutic desensitization stand against the theory that vernal catarrh is a manifestation of an allergic condition.

I believe that the forms described as "simple" and "follicular" are not true forms of vernal catarrh. They may be allergic conjunctivitis due to allergens (bacteria proteins, foods and pollens) in which eosinophils are usually present and which have seasonal incidence, or they are follicular conjunctivitis complicated by allergy.

The high percentage (50 per cent) of cases reported as instances of vernal catarrh associated with allergy would probably be reduced if a proper diagnosis were made in the first place.

In any event, a case in which there are no cobblestone vegetations should not be considered as one of vernal catarrh. In affirming that, I simply repeat what can be found in any textbook.

In conclusion, I believe that at present there is no better method of treatment for vernal catarrh than to destroy the vegetations with solid carbon dioxide. Though it is a rather lengthy process, it has the advantages of being harmless and of giving lasting results.

SUMMARY

Ten patients with vernal catarrh were treated with applications of solid carbon dioxide in a metallic container. In 9 cases the catarrh was of the tarsal type and in 1 of the limbic type. Generally, all persons responded favorably to this kind of therapy. In 2 cases (3 and 4) in which the results were not wholly successful, it must be noted that the number of treatments were insufficient, so that one cannot judge whether cure would have resulted if the patients had completed the treatments. The limbic types responded quickly to the treatments. The only patient with this type whom I treated was cured after six treatments. Some of the patients considered cured were followed for more than four years, without relapses being observed.

40 Fifth Avenue.

PARALYSIS OF DIVERGENCE

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AND
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Paralysis of divergence is a condition in which distant objects appear double. The diplopia, present with the eyes in the medial horizontal plane, does not increase when the test object is moved to either side. The double vision is homonymous and is less evident as the near point is approached.

The diplopia with paralysis of divergence is due to lack of divergence of the eyes which normally occurs when an object is viewed at a distance. This lack of divergence cannot be due to weakness of the external rectus muscles because there is no apparent impairment of their function. The most likely explanation of this disorder is that there is some disturbance of either the convergence or the divergence function. Exactly which of the mechanisms is involved is not yet clear. Since the two acts are antagonistic,[1] some investigators believe that divergence is merely a relaxation of convergence. This view is taken because the process of bringing the eyes inward is active and even voluntary, with an alleged center in the nucleus of Perlia. On the other hand, there is but slight motion during divergence, which actually is more than relaxation of convergence. A center for divergence has never been clearly demonstrated.

The following clinical and pathologic data were gathered from the study of a case in which the initial and major symptom was paralysis of divergence and in which at autopsy a single minute hemangioma was found in the periaqueductal central gray matter at the level between the superior and the inferior colliculi. The finding of this tumor lends considerable support to the theory that a center for divergence exists.

From the Neurologic Service and Laboratories of the Mount Sinai Hospital

1. The act of convergence is accomplished by a contraction of both internal rectus muscles. With this, there is a simultaneous relaxation of the external rectus muscles. The act of divergence is affected by contraction of the external rectus muscles and a concomitant relaxation of the internal rectus muscles. The convergence and divergence mechanisms are antagonistic and reciprocal in their actions.

REPORT OF A CASE

History.—An 18 year old student entered the Mount Sinai Hospital on July 2, 1934, because of headaches and double vision. Four weeks before her admission she had an attack of frontoparietal headache and projectile vomiting, which persisted for four days. She was free of symptoms for two weeks. Nine days before admission the headache and vomiting recurred. On June 25 she noted double vision at a distance.

Examination.—Examination did not reveal any disease of the internal organs. The blood pressure was 110 systolic and 70 diastolic. The deep reflexes on the right side were slightly more active than those on the left.

The optic disks were hyperemic, with grayish striation near the edges. There was no papilledema. The ocular movements were normal in all directions. There was no evidence of an isolated palsy of the ocular muscles, though at times there seemed to be a transient internal strabismus of each eye. On extreme lateral gaze, abduction was intact in each eye. There was homonymous diplopia when the patient gazed at objects at a distance. This was found in the horizontal plane directly in front and to each side. The images separated as the distance between the test object and the patient was increased. They did not separate, however, when the object was moved in the horizontal plane. This was evidently the diplopia of paralysis of divergence. It was not present in the lower near field. The pupils were equal and reacted to light and in accommodation. There was no nystagmus. The plotted visual fields were normal. A lumbar puncture showed an initial pressure of 200. After removal of 10 cc. of fluid, the final pressure was 140 mm. of water. The Ayala index was 7.0.[2] The spinal fluid was clear and colorless and had a total protein content of 38 mg. per cubic centimeter; the sugar content was 65 mg. per hundred cubic centimeters. There were 4 cells in the spinal fluid. The blood count and urinalysis gave normal results. The Wassermann tests of the blood and spinal fluid were negative. The pulse rate and temperature were normal.

Course.—The patient continued to complain of headaches, dizziness and burning of the eyes. The intensity with diplopia at a distance varied. The separation of the images was slow, and the diplopia appeared only after a few minutes of fixation. The patient improved during her stay in the hospital, and the diplopia disappeared. She was discharged from the hospital and observed in the follow-up clinic.

On October 25 she reported that she had headaches but no double vision. There was no change in the status.

On April 25, she complained of an occasional headache. The pupils were found to be widely dilated and reacted better on convergence than to light.

On October 24 there were no complaints. The neurologic status was normal.

On June 11, 1936, she saw red spots in the temporal side of the left visual field on two occasions.

On June 25 the attacks of headache, vomiting and blurred vision recurred. Examination showed impairment of convergence. The patient was advised to reenter the hospital.

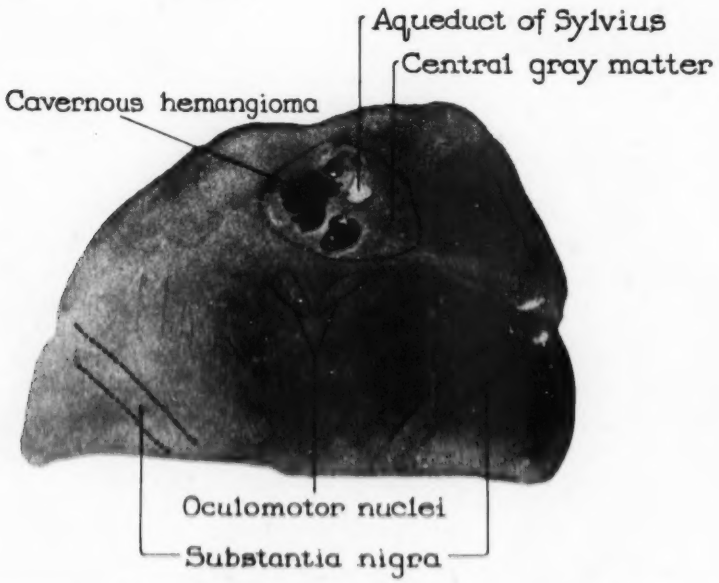
On July 2 the symptom of diplopia at a distance, from which she was free for two years, recurred. She began to lose weight. One week later the right and then the left eye turned inward. On July 16 there developed numbness and tingling of the cheek, and on July 27 the right foot felt numb and weak.

2. Ayala index $= \frac{\text{Final pressure}}{\text{Initial pressure}} \times 10.$

On July 30 the patient was readmitted to the hospital. Examination showed weakness of the right foot with right hyperreflexia. There were bilateral papilledema with hemorrhages. The peripheral visual fields were normal, but the blindspots were enlarged. The right pupil was slightly larger than the left. Both pupils reacted to light but better in accommodation. The right pupil was not as active as the left. There was a slight internal strabismus in the left eye, but there was no weakness of abduction in either eye. The ocular movements were good in all directions. A slight nystagmus was noted on upward gaze. The paralysis of divergence was present.

Lumbar puncture revealed the fluid to be under a pressure of 170 mm. of water. The Ayala index was 4.1. The caloric tests yielded normal responses.

All observers found the syndrome of paralysis of divergence but no weakness of the external rectus muscles.



Photograph of a section through the tegmen of the midbrain, enlarged three times, showing the size and position of the hemangioma in relation to the oculomotor nuclei. The maximum diameter of the hemangiomatous tumor was 4 mm.

A ventriculogram revealed symmetric internal hydrocephalus. Exploration of the posterior fossa showed no tumor. The patient died shortly after the operation.

Postmortem Examination.—Autopsy was done on August 7. The brain was sectioned by Dr. J. H. Globus, who reported the presence of marked internal hydrocephalus involving the entire ventricular system anterior to the fourth ventricle. The distention was symmetric. The vermis was found split by a linear operative incision down to the fourth ventricle. On either side of the incision there was an accumulation of coagulated blood. The roof of the fourth ventricle was disfigured and dislodged to the right.

The enlargement of the ventricular system anterior to the aqueduct in the presence of a nondilated fourth ventricle indicated an obstruction in the midbrain. Because of this, the brain stem directly caudad to the posterior commissure, where it communicates with the aqueduct of Sylvius, was cut, and a small bit of brown tissue was found to plug the opening.

Histologic preparation of the midbrain at this level showed the aqueduct to be distorted and enlarged by abnormal tissue. Serial sections of the rest of the brain stem disclosed no abnormalities. About the aqueduct there was a group of blood vessels, thin-walled vascular sinuses, as shown in the accompanying illustration. The walls were composed of connective tissue. Smaller vessel coats were thicker, and in some an internal elastic lamina could be discerned. The lumens were filled with blood and pigment granules. The vascular channels were separated by a dense collection of collagenous fibers. More peripherally, the vascular aggregation was surrounded by a zone of proliferated glia, which at some points ended in processes. The glia apparently was an extension of the subependymal area. Near the aqueduct was a small epithelium-lined cavity, apparently pinched off from the main pathway. More caudally, at the level of the trochlear nuclei, the aqueduct showed less obstruction and distortion. Many of the ganglion cells in the third and fourth cranial nuclei showed degenerative changes characterized by eccentricity, swelling and blurring of their nuclei. The abducens nuclei were normal.

The histologic diagnosis was cavernous hemangioma.

COMMENT

In 1883 Parinaud [3] first described the clinical picture of paralysis of divergence. Since then numerous instances have been reported. Straub [4] encountered paralysis of divergence associated with a tumor of the middle fossa. Holden [5] found it associated with a tumor of the midbrain. Howard [6] described it in a patient with carcinoma of the breast with metastasis to the region of the hypothetic divergence center. Necropsy was not performed in any of the cases. Howard aptly stated: "In such a case an autopsy following an early death might have given us some more definite clues than we now have regarding the location of the divergence center."

In some of the reported cases no etiologic factor is mentioned (Stokes [7] and Roese [8]). Bachstez,[9] Dor,[10] Sauvineau [11] and Dunning-

3. Parinaud, M. H.: Paralysie des mouvements associés des yeux, Arch. de neurol. **5**:145 (March) 1883.

4. Straub, M.: Ueber Lähmung der Divergenz, Centralbl. f. prakt. Augenh. **21**:8 (Jan.) 1897.

5. Holden, W. A.: The Ocular Manifestations of Epidemic Encephalitis, Arch. Ophth. **50**:106 (Jan.) 1921.

6. Howard, H. J.: Divergence Paralysis, Am. J. Ophth. **14**:736 (Aug.) 1931.

7. Stokes, W. H.: Paralysis of Divergence, Arch. Ophth. **11**:651 (April) 1934.

(Footnotes continued on next page)

ton [12] have observed this syndrome in cases of epidemic encephalitis. Vom Hofe,[13] Alger,[14] Zentmayer,[15] Lebensohn,[16] Duane [17] and Braunschweig [18] recorded it in cases of syphilis involving the central nervous system. Parinaud [3] and Dunphy [19] reported it in cases of multiple sclerosis. Cutler,[20] in discussing Wheeler's case, mentioned that he had observed the syndrome associated with anterior poliomyelitis. Alger [14] mentioned diphtheria and vascular disease of the brain stem as possible causes; Bielschowsky,[21] lead poisoning and head injury. Wheeler [22] postulated that hemorrhage into the region of the divergence center following exertion caused the condition. Lebensohn [16] mentioned a case in which chorea was present. Von Hippel [23] encountered the syndrome in a case of severe hysteria. Winawer [24] saw it in a person with a history of migraine of long standing.

The etiologic agents of paralysis of divergence are apparently varied, and little information could be obtained from the reported cases as to the location of the lesion. Our clinicopathologic study indicated that paralysis of divergence can be caused by a lesion in the tegmentum of the midbrain and favors the hypothesis that a divergence center

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8. Roese, H. F.: Ein Fall von sogenannter Divergenzlähmung, Klin. Monatsbl. f. Augenh. **90**:617 (May) 1933.

9. Bachstez, E.: Ueber Divergenzlähmung bei Encephalitis epidemica, Wien. med. Wchnschr. **75**:2501 (Nov.) 1925.

10. Dor, L.: Les troubles oculaires de l'encéphalite léthargique, Clin. opht. **24**: 17 (Jan.) 1920.

11. Sauvineau, C.: Symptômes oculaires et localisations cérébrales de l'encéphalite léthargique, Clin. opht. **24**:213 (May) 1920.

12. Dunnington, J. H.: Paralysis of Divergence with Report of Three Cases Due to Epidemic Encephalitis, Arch. Ophth. **52**:39 (Jan.) 1923.

13. vom Hofe, K.: Ueber Divergenzlähmung. Ztschr. f. Augenh. **61**:54 (Jan.) 1927.

14. Alger, E. M.: Paralysis of Divergence, Tr. Am. Ophth. Soc. **14**:665, 1916.

15. Zentmayer, W.: Report of a Case of Paralysis of Divergence, Tr. Am. Ophth. Soc. **13**:521, 1912.

16. Lebensohn, J. E.: Paralysis of Divergence with Chorea and with Tabes, Am. J. Ophth. **9**:684 (Sept.) 1926.

17. Duane, A.: Paralysis of Divergence, Ophthalmology **2**:11 (Oct.) 1906.

18. Braunschweig: Mischinfektion von Gonorhöe mit Diphtherie? Klin. Monatsbl. f. Augenh. (pt. 2) **46**:644, 1908.

19. Dunphy, E. B.: Paralysis of Divergence, Am. J. Ophth. **11**:298 (April) 1928.

20. Cutler, in discussion on Wheeler.[22]

21. Bielschowsky, A.: Ueber die sogenannte Divergenzlähmung, Ber. ü. d. Versamml. d. ophth. Gesellsch. **28**:110, 1900.

22. Wheeler, J. M.: Divergence Paralysis, Arch. Ophth. **47**:419, 1918.

23. von Hippel: Ueber Divergenzlähmung. München. med. Wchnschr. **49**:122, 1902.

24. Winawer, cited by Wilbrand, H., and Saenger, A.: Neurologie des Auges, Munich, J. F. Bergmann, 1921, vol. 8, p. 110.

exists. The possibility that the lesion in this region might act as an irritant of the center for convergence must be mentioned. The hemangioma in this case may have irritated the nuclei of convergence and produced a spasm, giving the clinical picture of paralysis or divergence. This hypothesis does not seem tenable, because patients with paralysis of divergence complain of continuous diplopia. It is hardly likely that there would be persistent irritation and spasm without occasional relaxation due to fatigue.

There is some experimental proof for the existence of a divergence center. One of us (M. B. B.) found that electric stimulation of the cortex of a monkey at the parieto-occipital junction produces some divergence of the eyeballs and miosis. This divergence of the eyes must be mediated through a lower nuclear center which coordinates the movement for divergence. This is presumptive evidence that a center for divergence exists in primates. Any pathologic process which involves the area of the brain where the center exists, that is, in the midbrain, will produce a paralysis of divergence. In the case reported in this paper such a center was more precisely localized in the brain stem in the central gray matter and periaqueductal region at the level between the inferior and the superior colliculi.

Whichever theory is correct, all that one can conclude from this clinicopathologic presentation is that paralysis of divergence can be caused by a small cavernous hemangioma localized in the periaqueductal central gray matter at the level of the lower portion of the oculomotor nuclei.

SUMMARY

A case is described in which the first symptom, and the only one during most of the clinical course, was paralysis of divergence and in which at autopsy a small cavernous hemangioma was found in the tegmen of the midbrain.

CHORIORETINAL ARTERIOLAR NECROSIS IN MALIGNANT HYPERTENSION

REPORT OF A CASE

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The association of lesions of the fundus with hypertensive vascular diseases has been the subject of many papers during the past few years. The clinical significance of this association and its varied interpretation by internists, pathologists and ophthalmologists warrant further investigations and reports in order that the correlation may be better understood.

For an intelligent interpretation of lesions of the fundus observed in cases of hypertensive vascular disease, information is necessary concerning the onset of hypertension, i. e., whether it is mild and gradual, extending over a long period, or acute and accelerated; the systolic and diastolic blood pressure readings; the results of urinalysis and studies of the blood chemistry; the presence of persistent headaches, nausea and visual disturbances, and a history of hereditary hypertension.

The lesions may be stationary, progressive or retrogressive, or there may be remissions, depending on the degree and consistency of elevation of the systolic and diastolic blood pressure and also on the arteriolar involvement of other vital organs, especially kidneys, brain or heart. Sclerosis is a selective process which may involve parts of vessel walls in various areas of the vascular bed. The internist will find the retinal sclerosis an important diagnostic and prognostic guide, since the retinal and choroidal vasculature and its surrounding tissue may be directly observed in a way not possible in any other organ.

Some internists regard so-called benign and malignant hypertension as separate entities, while others consider hypertension a single entity of varying degrees of severity. In several cases under my observation over a period of ten years, the "benign" form of "essential" hypertension existed for eight or nine years and then developed into an accelerated phase, or "malignant" hypertension. Whether this accelerated phase

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represents another disease superimposed on the "benign" hypertension or whether it is a prolongation of the "benign" form is still under investigation. Extensive records of lesions of the fundus during the protracted course of hypertension may be valuable in the solution of this phase of the problem.

"Essential" hypertension is regarded by most authorities as a clinical entity, other diseases not being present to an extent sufficient to account for the symptom of the markedly and persistently increased blood pressure. Angiospasm of the arterioles of the eye and other organs, particularly the kidney, has been regarded as the initial factor in the narrowing of the lumens of these vessels, which may eventually result in sclerosis. Some authors consider that the spasm is caused by a vasomotor disturbance due to hyperfunction of the adrenal and other glands, while others maintain that it is due to a toxic factor, such as that observed in toxemia of pregnancy.

"Essential" hypertension is of unknown origin and is generally described as existing in two forms, namely, the "benign" and the "malignant." Patients with the "benign" form may enjoy normal health for many years without discomfort and without requiring treatment. The fundus is often devoid of any lesion, although in some cases it will show a mild localized arteriolar sclerosis, marked by slight attenuation of the small arteries or arterioles, moderate venous engorgement, arching or kinking of the veins due to the arteriolar venous compression and sometimes, although rarely, a few hemorrhages or exudates. The sclerosis is a permanent lesion, while the angiospasm is functional and transitory. The hemorrhages and exudates are generally resorbed, leaving no residue. This form of hypertension shows no marked lesion of the fundus, such as edema of the disk or the retina or numerous hemorrhages or exudates. The vascular pathologic process consists of diffuse hyperplastic or hyaline degeneration of the arterioles without necrosis of the vessel walls.

"Malignant" hypertension is generally considered an independent disease of unknown origin, characterized by an acute onset of systemic hypertension with a high diastolic blood pressure, occurring in young and in middle-aged persons. It is a diffuse arteriolar lesion, in which an arteriolar necrosis is frequently the outstanding feature (Klemperer and Otani [1]). Colored photomicrographs illustrating the changes in "malignant" hypertension associated with chorioretinal arteriolar necrosis are presented with the subsequent case report. The arteriolar necrosis

1. Klemperer, P., and Otani, S.: "Malignant Nephrosclerosis" (Fahr), Arch. Path. **11**:60 (Jan.) 1931.

was not evident in sections of any other organ. This retinal lesion is called by Wagener [2] "retinitis of malignant hypertension."

"Malignant" hypertension is a serious malady, because the brain, heart and kidneys generally become involved. Visual disturbances and lesions of the fundus are almost always early signs. I have found that the lesions of the fundus may be either moderate or severe, at times progressing from the moderate to the severe form. The characteristic lesions in the two forms of hypertension are as follows: The optic disk is at first hyperemic; later the disk and the surrounding retina may be edematous, owing to the chorioretinal sclerosis with ischemia. The retinal venules are engorged and tortuous; the arterioles are contracted and tortuous and show a prominent central light reflex. The veins are arched and compressed where they are crossed by sclerosed arterioles. There may be a localized retinal venous thrombosis and hemorrhages, grayish, ill defined exudates or necrotic foci, a partial or complete star figure in the macular area, subchoroidal or vitreous hemorrhages and, rarely, detachment of the retina or choroid beading or embolism of the central artery. Marked edema of the disk and the surrounding retina characterizes the severe form of "malignant" hypertension and usually signifies serious involvement of vital organs, especially the kidneys and brain, as stated in a previous article by me.[3]

Both eyes may show these pathologic changes in varying degrees. The prognosis is grave, especially in the young. Death is due to renal, cerebral or cardiac failure and occurs as a rule several years after the appearance of the moderate form of lesion of the fundus and generally several weeks or months after the severe form.

Local ocular treatment is of no avail. General treatment is directed to the cardiac, cerebral and renal conditions.

If a mild protracted hypertension is accompanied by renal involvement, the fundus may show lesions indicative of an arteriolar sclerotic kidney, that is, a primary contracted kidney or benign nephrosclerosis. Lesions observed in the severe form of chronic diffuse glomerular nephritis with severe hypertension may simulate the fundus picture seen in "malignant" hypertension. A previous history of hypertension or nephritis may assist in the differentiation.

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2. Wagener, H. P.: The Retinitis of Malignant Hypertension, Tr. Am. Ophth. Soc. **25**:349, 1927.

3. Cohen, M.: Significance of Pathologic Changes in Fundus in General Arterial and Kidney Diseases, Tr. Sect. Ophth., A. M. A., 1922, p. 60; abstracted. J. A. M. A. **78**:1694 (June 3) 1922.

The changes in the fundus frequently observed in the toxemia of pregnancy are due to toxemia, hypertension or a complicating nephritis. The fundus may be free from any lesion, or it may present moderate or severe "malignant" hypertensive lesions with angiospasm of the retinal arterioles in isolated areas. After delivery, these manifestations often disappear, leaving no residue unless the condition is complicated by severe nephritis.

Arteriosclerosis is a vascular lesion of unknown origin occurring in the aged. It affects the arterial walls of large blood vessels in contradistinction to a primary involvement of smaller vessels seen in arteriolar sclerosis. Arteriosclerosis extends to the smaller arteries and arterioles in the retina. Diversified sclerotic lesions of the general vasculature, particularly the brain, may accompany the retinal sclerosis. The fundus is frequently normal. If a "benign" or "malignant" hypertension intervenes, the changes in the fundus will be similar to those observed in "benign" or "malignant" hypertension.

Diabetes mellitus is a disease of young and middle-aged persons. In this condition lesions of the fundus are frequently evident in the middle aged in connection with arteriosclerosis. The lesions of the fundus in so-called diabetic retinitis are the result primarily of the arteriosclerosis, a degenerative lesion, and secondarily of protracted glycosuria. If hypertension accompanies diabetes mellitus, the fundus may assume, in addition, the vascular lesions observed in "benign" or "malignant" hypertension.

REPORT OF CASE

History.—P. J., a Negro 40 years of age, a clerk, was admitted to the Broad Street Hospital on Oct. 1, 1937, to the service of Dr. Herbert Wiener, who requested me to make an ophthalmoscopic examination on October 7. The patient had been married for two years but had no children; his wife had had no miscarriages. His father died at the age of 55, of cerebral hemorrhage, and his mother and two sisters were living and well. He was well nourished. He had had the usual diseases of childhood, but did not give a history of syphilis. He drank and smoked heavily.

In August 1937 he had two epileptic seizures, for which he was treated at the Kings County Hospital. His average blood pressure was 280 systolic and 180 diastolic. His heart was enlarged, but there were no murmurs. The abdomen was distended. There was no edema of the legs. Examination of the fundi showed elevation of the disks and recent hemorrhages.

A diagnosis was made of malignant hypertension (essential) and hypertensive encephalopathy.

On admission to the Broad Street Hospital he complained of recurrent attacks of epileptiform seizures, occasional right hemianopia with mental confusion at times, headaches, blurred vision and occasional diplopia for the past year and frequency of micturition for two months.

EXPLANATION OF FIGURE 1

Fig. 1.—*A*, a drawing of the fundus. A description is contained in the case report.

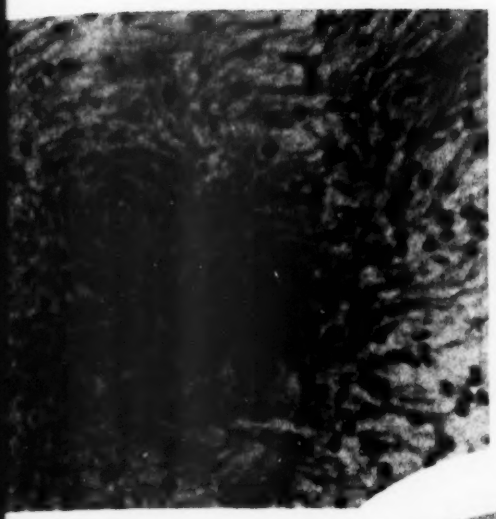
B, photomicrograph of the retina showing edematous tissue. An arteriolar wall is thickened and has a smudgy appearance due to necrosis; an adjoining arteriole shows proliferation of endothelium into the lumen. Hematoxylin and eosin stain; × 250.

C, photomicrograph of the retina showing edema. An arteriole shows marked proliferation of endothelium into the lumen; the adjoining vein is dilated. Hematoxylin and eosin stain; × 250.

D, photomicrograph of the choroid (taken from the same serial section as *B*). Three arterioles are seen with thickened smudgy walls, indicating necrosis causing practically complete occlusion of the lumens. The arteriole in the center also shows proliferation of endothelial cells. Hematoxylin and eosin stain; × 250.

E, photomicrograph of the choroid (taken from same serial section as 2 *C*). This area shows two choroidal vessels with thickened necrotic walls having the characteristic purplish color seen in necrosis; a few foam cells permeate the walls; the lumens are narrowed and contain proliferated endothelial cells. Hematoxylin and eosin stain; × 250.

A, *B* and *C* were prepared by the Dufay process. *D* and *E* were prepared by the Kodachrome process in order to insure accurate reproductions of the stained microscopic sections.



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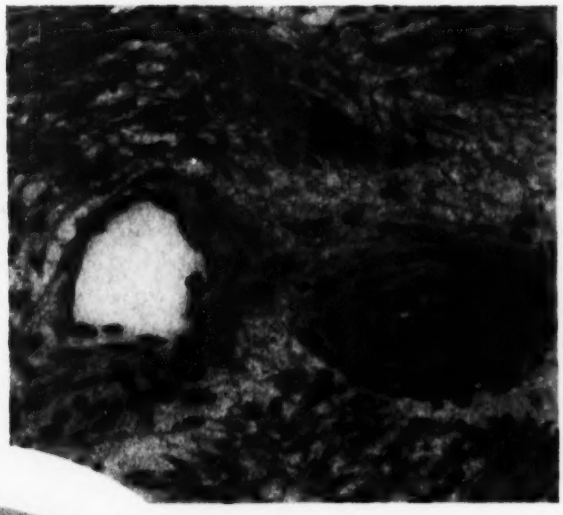

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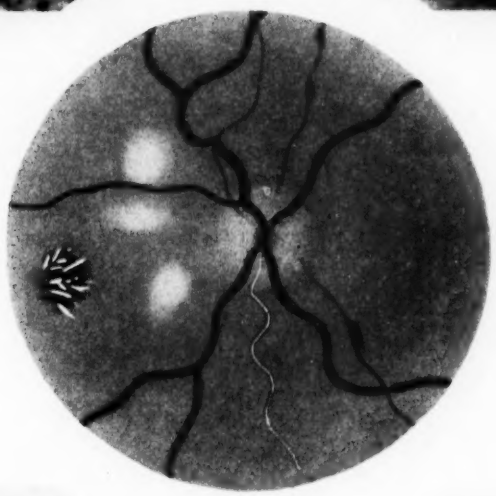


A

D

E

Fig. 1.

Explanation of Figure 2

Fig. 2.—*A*, photomicrograph of the choroid (taken from the same serial section as figure 2 *D*). The two choroidal arterioles show a marked proliferation of fibrous tissue between the lumen and the internal elastica, causing encroachment on the lumen. The internal elastica of both vessels is reduplicated and split, signifying arteriolar sclerosis. Weigert's elastic tissue stain; × 250.

B, photomicrograph of the choroid (taken from the same serial section as figure 2 *D*). Two choroidal arterioles with their elastica are seen; one shows the lumen completely occluded, illustrating an arteriolar occlusion due to fibrosis; in the other, the lumen is practically occluded. Weigert's elastic tissue stain; × 250.

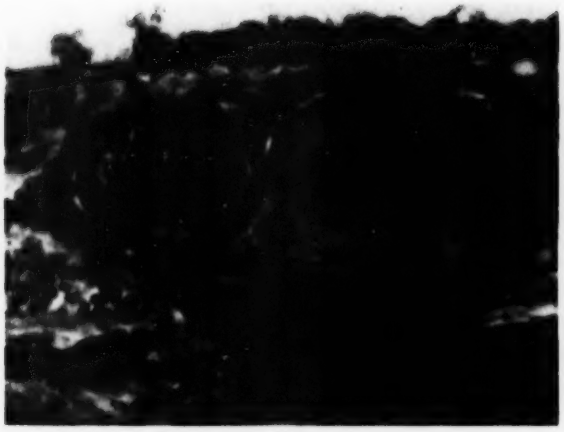
C, photomicrograph of the posterior segment of the eye. The retina shows sclerotic arterioles, necrotic foci, hemorrhages and fibrinous exudates; the choroid and sclera show hyalinization of the vessel walls. Hematoxylin and eosin stain; × 20.

D, photomicrograph of the posterior segment of the eye. There are edema of the disk and surrounding retina, dilatation of veins and sclerosed arterioles. Weigert's elastic tissue stain; × 20.

E, photomicrograph of the kidney. A focal area of cortical fibrosis is shown in which there is a normal glomerulus and also one showing a partial fibrosis. The intervening parenchyma shows little or no change. There are distinct vascular changes, namely, marked subendothelial hyalinization of the arterioles producing definite thickening of the walls with marked encroachment on the lumens. Hematoxylin and eosin stain; × 250.

These pictures were prepared by the Kodachrome process in order to insure accurate reproductions of the stained microscopic sections.

A



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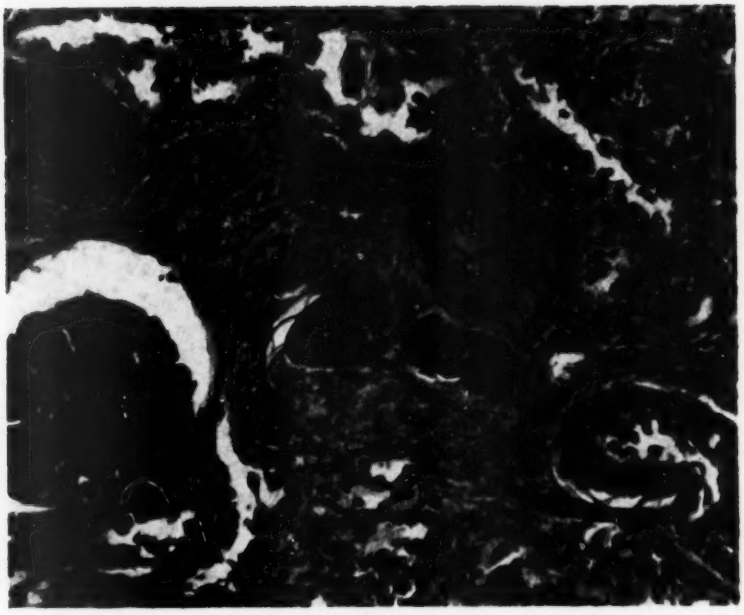
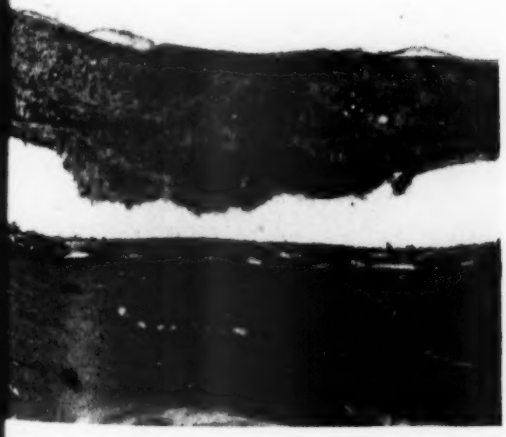


E



C

D

Fig. 2.

UNIV. OF MICH.

Examination.—His average blood pressure for ten days was 278 systolic and 158 diastolic. His heart was enlarged; there were no murmurs. The Wassermann and Kahn reactions were negative. The specific gravity of the urine varied from 1.010 to 1.025; albumin was found (2 plus), and 2 to 3 red blood cells and hyaline and granular casts were seen. The nonprotein nitrogen content was 34 mg. per hundred cubic centimeters, and the urea nitrogen content 25 mg. These findings indicate that the function of the kidney was not impaired.

Examination of the Fundi.—Examination of the fundus of the right and the left eye (fig. 1 *A*) disclosed practically identical findings. These consisted in edema of the disk in the state of retrogression from a choked disk, edema of the retina surrounding the disk, a few flame-shaped hemorrhages and a few isolated exudates or necrotic foci. The retinal veins were engorged and compressed; many of the retinal arteries were not visible, owing either to their marked attenuation or to retinal edema. In the macular area there were several radiating yellowish degenerative foci bordered by pigment. The fundus condition was diagnosed as retrogressive edema of the papilla, edema of the retina and retinal arteriolar sclerosis.

Course.—After a few days the patient became comatose. Hemiplegia developed on the left side, and the patient died on the tenth day after admission. An autopsy was permitted and was performed by Dr. Gonzales. All of the organs, including the eyes, were studied.

A diagnosis of massive cerebral hemorrhage and marked arteriosclerosis was made on the basis of the macroscopic observations.

Histologic Ocular Examination.—After the eyes were hardened, serial sections were made and stained with hematoxylin and eosin and with Weigert's elastic tissue stain. Examination disclosed practically identical changes in the two eyes.

Retina: The retinal tissue showed edema and swelling, particularly of the disk and the adjacent area (fig. 2 *D*), with a number of focal hemorrhages and exudates. There was hyaline thickening of the walls of the small arterioles with distinct narrowing of the lumen in places. One vessel showed necrosis of its wall (fig. 1 *B*); another showed endothelial proliferation (fig. 1 *C*).

Choroid: The choriocapillaris was essentially normal. The choroidal veins were not altered except for decided dilatation. The smaller arteries showed distinct intimal proliferation and, in places, endothelial proliferation with consequent marked narrowing and obliteration of the lumens. In some of the sections there was definite arteriolar necrosis with complete obliteration of the lumen. Within the necrotic walls (fig. 1 *D* and *E*) were vacuolar spaces, possibly foam cells, the appearance of which suggested an accumulation of lipoid material. The purplish and smudgy color of the arteriolar walls was significant of necrosis. One section showed a localized area of hemorrhage in the intervascular space. The choroidal pigment appeared essentially normal. The choroid itself appeared thickened. Staining with Weigert's elastic tissue stain revealed the characteristic splitting and reduplication of the elastic lamina in some of the vessels (fig. 2 *A*) and also arteriolar occlusion due to fibrosis (fig. 2 *B*).

Sclera: The scleral vessels (fig. 2 *C*) showed hyaline changes similar to those in the choroid.

The posterior ciliary vessels were moderately thickened with some narrowing of the lumens. The central artery and vein were normal. The arachnoid membrane showed sclerosis of an arteriole.

A histologic diagnosis was made of edema of the disk and retina with chorioretinal arteriolar sclerosis and necrosis.

Summary: The most conspicuous changes in the eye, aside from the retinal edema and hemorrhages, were those in the arterioles and small arteries, producing arteriolar hyalinization and intimal thickening with distinct narrowing of the lumens. One vessel in the retina showed necrosis of the wall and practically complete obliteration of the lumen; similar lesions were seen in the choroid but to a more marked degree. No inflammatory reaction was present.

Microscopic Examination of the Viscera.—Kidney: There were a number of focal areas of cortical fibrosis with slight lymphocytic infiltration. In and adjacent to these areas a few of the glomeruli showed partial fibrosis. The intervening parenchyma, however, displayed little or no change. There were distinct vascular changes throughout the section, chiefly subendothelial hyalinization of the arterioles, producing a narrowing of the lumens, in some places to a marked degree. No arteriolar necroses were noted. There was moderate intimal proliferation of some of the medium-sized arteries. In general, however, the larger arteries were not conspicuously changed; most glomeruli were normal in appearance.

The general picture (fig. 2*E*) was that of advanced arteriolar sclerosis as seen in cases of marked hypertension in which uremia is not the cause of death.

Heart: The myocardial fibers were fragmented and torn. The connective tissue was increased, especially about the smaller blood vessels. Many of the small blood vessels had obliterated lumens and thickened hyalinized walls.

Basilar Vessels: Atherosclerosis was present.

Aorta: The intima was irregularly thickened. A large plaque formed of loose connective tissue containing many cholesterol crystals and vacuoles (previously holding lipoid material) could be seen projecting into the lumen (atherosclerosis).

Liver: The arterioles in the capsules showed similar thickening of the walls and obliteration of the lumens. The parenchyma showed no fibrotic replacement, its nutrition being derived mainly from venous sources.

Spleen: The walls of the arterioles were definitely thickened and the lumens practically obliterated. The lymph follicles were normal in structure.

Pancreas: There was a thickening of the walls of smaller vessels and a minimal fibrosis.

Miscellaneous: Brain tissue, voluntary muscle, adrenal gland and lung tissue showed normal vasculature.

SUMMARY

The interpretation of the lesions of the fundus in essential hypertension is invaluable in the diagnosis and prognosis of hypertensive vascular disease.

The lesions of the fundus in "malignant" hypertension have been observed in both the moderate and the severe form. The moderate form

differs ophthalmoscopically and clinically from "benign" hypertension and also from the severe form of "malignant" hypertension.

Histologic studies of serial sections of the eyes and other organs are essential for the detection of any degenerative vascular lesion.

The condition in the case reported represents the severe form of "malignant" hypertension, as made evident by the ophthalmoscopic, clinical and microscopic observations of chorioretinal arteriolar necrosis.

The observations in this case clearly demonstrate the fact that arteriolar necrosis of the retina and choroid may occur in the absence of similar vascular changes in the kidney or in any other organ.

DISCUSSION

DR. SAMUEL DONALD LEWIS: I should like to ask Dr. Cohen whether he distinguishes between benign hypertension and the malignant type only by the presence of edema of the optic disk and whether he has found all the other changes in the benign type?

DR. MARTIN COHEN: The difference between benign hypertension and the malignant form from the clinical and the ophthalmoscopic standpoint is readily distinguished. The lesion in the fundus in the benign type, as stated in the paper, is mild. It is only the severe form of malignant hypertension in which marked edema of the disk and the surrounding retina is present.

Clinical Notes

A NEW DETERGENT FOR USE IN THE PREOPERATIVE CLEAN-UP OF THE EYES

ROY O. SCHOLZ, M.D., BALTIMORE

The preoperative clean-up of eyes presents a problem somewhat different from that encountered in other parts of the body. The looseness of the skin of the lids makes penetration of the crevices difficult, and the sensitivity of the cornea and conjunctiva precludes the use of substances which are irritating when accidentaly instilled into the conjunctival sac. A new detergent composed of a mixture of sulfonated alcohols has recently become available as a cleansing agent. It possesses superior detergent properties and lowered irritability as compared with soap. This compound has been used for several months in routine preoperative clean-up of the lids, brow and adjacent skin at the Wilmer Ophthalmological Institute of the Johns Hopkins Hospital. Experimental and clinical results indicate that its use is preferable to the use of soap.

The irritant properties of ordinary soaps [1] may be due to the excess alkali present or to the type of fatty acids used. The irritation of the skin increases as the p_H of the solution or the molecular weight of the fatty acids is increased. Soaps function merely as a lubricant in the preparation of the skin, the number of bacteria removed depending on the mechanical force used rather than on the composition of the soap.[2] In cleaning up for ophthalmic operations superfatted soaps have found favor mainly because they have a low equivalent of alkali and are therefore relatively less irritant to the skin. However, even these soaps have a p_H of about 9.5 and do cause irritation when small quantities are accidentally instilled into the conjunctival sac. Soaps have the further disadvantage of precipitating calcium and magnesium in hard water, which greatly impairs their detergent properties.

A group of stable, neutral detergents are available [3] in the sulfonated alcohols. In an aqueous solution these products form a soaplike

From the Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital.

1. Gardiner, F.: Soaps and Their Effects on the Skin, Edinburgh M. J. **8**:514, 1912. Blank, I. H.: Action of Soap on the Skin, Arch. Dermat. & Syph. **39**:811 (May) 1939.

2. Price, P. B.: Bacteriology of Normal Skin: New Quantitative Test Applied to Study of Bacterial Flora and Disinfectant Action of Mechanical Cleansing, J. Infect. Dis. **63**:301, 1938.

3. Schrauth, W.: Die Höhermolekulären Alkohole der Fettreiher und ihre technische Bedeutung, Chem. Ztg. **55**:3 and 17, 1931.

liquid which is devoid of excess alkalinity and which will not precipitate calcium or magnesium. The particular detergent being used is an aqueous solution of sulfonated alcohols of higher molecular weights adjusted to a p_H of 6.8. It has a surface tension of only 37 dynes, which enables it to penetrate thoroughly the small crevices of the loose skin of the lids. Experiments performed in the department of

A, right eye of a rabbit before a drop of castile soap preparation was used; *B*, same eye seven hours later, showing exudate, and *C*, same eye thirty-six hours later, after staining with fluorescein. *D*, left eye of the same rabbit before a drop of the new chemical detergent was instilled; *E*, the eye seven hours later, and *F*, the eye thirty-six hours later, after staining with fluorescein.

surgery of the hospital [4] have demonstrated that this detergent removes slightly more of the flora of the skin than does soft soap and in brush burns and open wounds produces much less pain than does any soap.

4. Firor, W. M., and Brewer, J.: Personal communication to the author.

To study the effects of the detergent on the cornea and conjunctiva, the following experiments were performed:

One drop of the castile soap preparation formerly used in the clean-up in the Wilmer Ophthalmological Institute was instilled in the right eyes of 15 normal rabbits at the same time that a drop of the detergent was placed in the left eyes. There was an immediate reaction in the conjunctiva of both eyes of each rabbit. At the end of seven hours the right eyes showed progressive inflammation of the conjunctiva and corneal clouding, while the left eyes were beginning to clear. After thirty-six hours the right eyes took a marked superficial stain with fluorescein, while the left showed little or no stain, as shown in the accompanying illustration.

In preoperative preparations at the Wilmer Ophthalmological Institute the lids, brow and adjacent skin are scrubbed once the evening before and again on the morning of operation. A small amount of the cleansing agent almost invariably gets into the conjunctival sac during the course of this clean-up. During the period in which the sulfonated oil detergent has been used instead of soap the patients have shown less conjunctival irritation than they did when castile soap was employed.

In view of its better detergent properties, neutrality and lessened irritability, this sulfonated alcohol detergent is probably superior to the soaps commonly used in preoperative ophthalmic preparations of the skin.

Ophthalmologic Reviews

EDITED BY DR. FRANCIS HEED ADLER

CONGENITAL AND ACQUIRED ANOMALIES OF THE OPTIC DISK

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SAN FRANCISCO

The examination of the optic nerve is an important part of every examination of the fundus. In attempting to determine whether or not a pathologic process is present, it is essential that the normal disk and its variations, as well as the congenital anomalies, be thoroughly understood. For this reason the major portion of this review will be devoted to the normal disk and its congenital variations.

THE NORMAL DISK AND ITS ANOMALIES

In the examination of a disk a certain routine has become a fixed habit. This routine will be adhered to in the following discussion.

Media.—It is important that the media be examined before observing the fundus. Fine opacities in the cornea, lens or vitreous may cause relatively little loss of vision and yet be sufficient to interfere with the detailed examination of the disk. In addition, the presence of these opacities has a tendency to make the disk assume a redder color than normal.

Size and Shape.—The optic disk is 1.5 mm. in diameter. The variations in size as seen with the ophthalmoscope are only apparent in most instances. In the hyperopic eye the disk appears smaller than normal, as best illustrated by the disk of an aphakic eye. In the myopic eye, on the other hand, the disk appears to be definitely larger than normal. True differences in size, however, are met with, as illustrated by the unusually small papillae sometimes encountered in the "little" hypermetropic eye.

In form, the normal disk is usually round or slightly oval vertically. At times it may appear to be elongated horizontally or obliquely as the result of a high degree of astigmatism. When this is true it is not possible to have the entire disk in focus at the same time. When either the long or the short axis is in focus the opposite one will be blurred a varying amount, depending on the degree of astigmatism present.

Color of the Disk.—The color of the normal disk of youth has been variously described as ranging from orange pink to a peach blossom pink, with the temporal side a little brighter than the nasal. The color results from the combination of that of the lamina cribrosa and its meshes with that of the almost transparent fibers of the optic nerve. The former is almost white, except for the apertures, while the optic nerve fibers, which are slightly gray, seem reddish, owing to the presence of numerous capillaries. Where the fibers are more closely packed, as at the nasal side, the disk appears redder, while the temporal portion with its fewer fibers of the papillomacular bundle appears

Fig. 1.—Scleral ring. (All of the illustrations in this paper were photographed from W. W. Wilmer's "Atlas Fundus Oculi" by permission of the publisher, The Macmillan Company, of New York. This illustration was plate 93 of the original text.)

decidedly paler. In the floor of large physiologic cups in which there are few fibers the color is white, the color of the lamina cribrosa. In old age the reddish color of the disk is displaced by a yellowish hue.

The color of the disk is also influenced by the surrounding retina. In the more heavily pigmented fundus the disk appears bright or light, while in the blond type of fundus it is redder. This is especially well illustrated in the albinotic fundus.

Abnormalities of color are seen in disease. In the presence of inflammation or congestion the disk is redder than normal, while in case of

atrophy it becomes pale. These variations will be further considered under diseases of the optic nerve.

Margin of the Disk.—The edges of the normal disk are clearcut, with the nasal edge less distinct than the temporal border because of the greater number of nerve fibers that pass over the nasal border. Any blurring of the margin of the disk is due to congenital anomalies, edema, inflammation or postinflammatory changes. Some of these congenital anomalies are described.

Scleral Ring: This consists of a small white line at the border of the disk and results from scleral bundles jutting in between the margin of the choroid and the disk. It has also been called a glial ring (fig. 1).

Pigment (Choroidal) Ring: At times a narrow ring of pigment surrounds a portion of the margin of the disk. This is the result of a piling up of the pigment epithelium. It is usually sharper on the temporal side due to the presence of fewer nerve fibers. It may border the disk at any place or completely surround it. Any pigment that seams the disk is not pathologic (fig. 2).

Scleral Crescent (Temporal Conus): The sides of the wall of the scleral hole may be oblique, so that a portion of the wall of this opening is seen, making a white crescent and giving the disk the appearance of being narrowed vertically. It is found most frequently at the temporal side, and according to Wilmer [1] it is apt to increase with age (fig. 3).

Choroidal Crescent or Conus: The pigment epithelium may at times not quite reach the scleral opening. This produces a crescent of lighter color in which the choroidal circulation is often visible. At times a large physiologic cup opening toward the temporal side may show a crescent of choroidal vessels. Johnson [2] stated that it may be difficult to determine whether these vessels really lie on the disk or alongside it.

Staphyloma Posticum: This condition is similar to the choroidal crescent and is due to a stretching out as the result of myopia. The retinal epithelium undergoes atrophy, so that the choroidal vessels also, as a rule, show some changes. When the condition is advanced there is a white crescent not unlike the inferior conus. The latter, however, is present at birth and is stationary throughout life. It is unaccompanied by signs of degenerative changes in the eye and is usually associated with hyperopia. The crescent associated with myopia is temporal or annular in 90 per cent of the cases. Wilmer [1] stated that the increase

1. Wilmer, W. W.: Atlas Fundus Oculi, New York, The Macmillan Company, 1934, p. 28.

2. Johnson, G. L., and Head, A. W.: Pocket Atlas and Text-Book of the Fundus Oculi, ed. 2, London, Adlard & Son, Ltd., 1931, p. 146.

Fig. 2.—Incomplete choroidal ring. (From Wilmer,[1] plate 90.)

Fig. 3.—Scleral crescent. (From Wilmer,[1] plate 7.)

or nonincrease in extent of this conus indicates the tendency of the myopia to progress or to remain stationary (fig. 4).

Double Conus: This anomaly consists of an inner lighter crescent and an adjacent outer more or less dark gray crescent. The latter zone is choroidal in origin. It is usually found at the temporal side and may be associated with a scleral ring.

Inferior Conus: This condition consists of a white crescent situated at the lower or lower temporal border of the disk and is ⅛ or ⅓ disk diameter in size. There is usually a depressed pale physiologic cup, at the bottom of which the lamina cribrosa can be seen and from which the

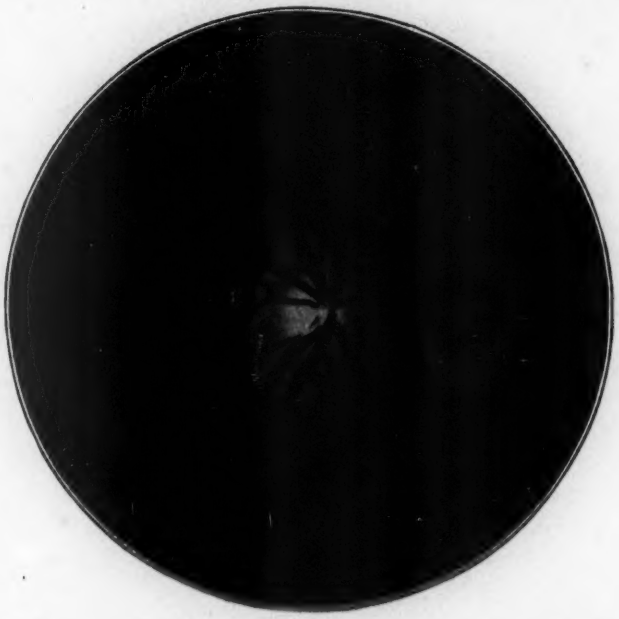

Fig. 4.—Staphyloma posticum. (From Wilmer,[1] plate 5.)

vessels emerge. The disk is oval, with long axis parallel to the conus. The condition is usually accompanied by defective vision, which is often the result of a refractive error. While myopia may occur, hyperopic astigmatism is the rule. Worton[3] pointed out that the axis of the astigmatism usually corresponds with the direction of the conus. As early as 1885 Vossius[4] found that inferior conus was directly below the disk in 67 per cent of the cases.

Tertsch[5] demonstrated microscopically that the appearance is due to a deficiency of the choroid. Bruch's membrane, the pigment epi-

3. Worton, A. S.: Ophthalmoscope **9**:833, 1911.
4. Vossius, A.: Klin. Monatsbl. f. Augenh. **23**:137, 1885.
5. Tertsch, R.: Arch. f. Ophth. **84**:530, 1913.

thelium and the nuclear layers of the retina fail to reach the edge of the disk, while the sclera itself is usually thinned in the area of the conus.

The condition of conus was attributed by Schnabel [6] to defective closure of the fetal cleft. Fuchs [7] agreed with this and discussed the difference between this condition and the acquired conus of myopia, which is due to atrophy of the choroid. As a result of this article, inferior conus is also known as Fuchs's coloboma. There has been considerable controversy as to whether the condition is primarily a beginning coloboma or whether it is due to imperfect development with giving way and stretching under the influence of intraocular pressure. Mann [8] suggested that the primary aberration is due to a failure in the development of the pigment epithelium near the disk, the failure being probably of the nature of a metaplasia.

Venous Sling: Coats,[9] von Szily [10] and others have reported as a further variation in inferior conus, the venous sling. In this anomaly the vein runs forward to the edge of the coloboma, turns sharply under the retina and then returns to the optic cup. This may be associated with scleral ectasia, as, in addition to the lack of choroid already mentioned, the sclera in these cases is often thinner in this area.

Inversio Papillae: The vessels and vessel cone may be directed sharply to the nasal side or below rather than being located in the center and sloping to the temporal side. This produces a characteristic picture that suggests conus. At times this inversion of the papilla may be associated with inferior conus.

Coloboma of the Disk: There are two distinct types of this anomaly. The first type is limited to the disk. It is closely related to the congenital crescent and the physiologic cup. Colobomas of this type are extremely diverse in appearance, no two being exactly alike. Their origin may be traced to some interference with the complete closure of the fetal ocular cleft or with some investment of the scleral sheath around the papilla. They may involve only a portion of the disk. When this occurs the disk is excavated at its lower part, and the vessels are seen to curl over the edge in a manner similar to that seen in a glaucomatous cup. In such instances the vessels emerge in an irregular fashion (fig. 5).

The second and best known form of coloboma is that in which the entire disk is involved and in which there is also a coloboma of the choroid. Ophthalmoscopically, there is a white patch around the disk, while below it there is a further oval, round or irregularly shaped patch

6. Schnabel, J.: Arch. f. Ophth. (pt. 2) **20**:1, 1874.
7. Fuchs, E.: Arch. f. Ophth. (pt. 1) **28**:139, 1882.
8. Mann, I.: Brit. J. Ophth. **7**:359, 1923.
9. Coats, G.: Ophthalmoscope **12**:400, 1914.
10. von Szily, A.: Arch. f. Ophth. **110**:183, 1922.

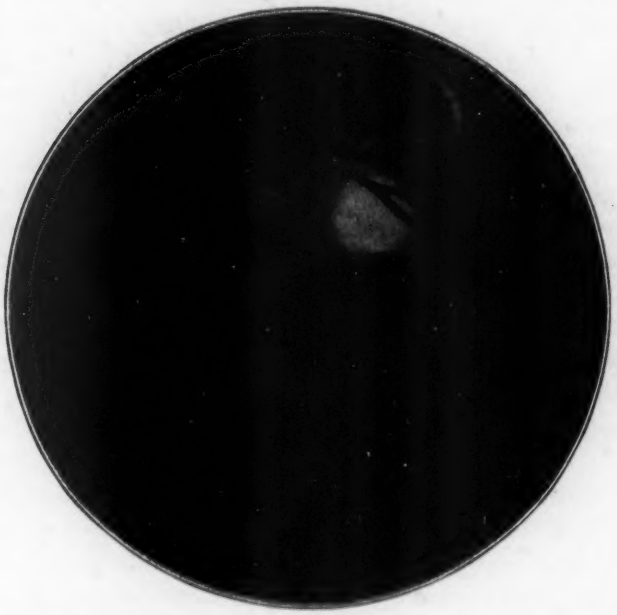

Fig. 5.—Small coloboma in the lower portion of the disk. (From Wilmer,[1] plate 18.)

Fig. 6.—Congenital pit in the optic disk. (From Wilmer,[1] plate 95.)

which may be almost any size. In these cases the nerve tissue occupies the upper portion of the greatly enlarged disk. The vessels vary a great deal and may emerge from the lower part of the pseudodisk or from the center or they may appear at the edges around the entire circumference.

Another type of coloboma is that of a normal papilla in the floor of a cylindric regular deep pit, which may have a depth of 9 diopters. Stock and von Szily [11] expressed doubt whether this is a true coloboma and have given the condition the name of staphyloma verum peripapillare.

Pits in the Optic Disk: These crater-like holes, as a rule, appear in the lower temporal part of the disk, are ⅛ to ⅙ disk diameter in size and gray to olive green in color. Vessels often emerge from or enter the hole. Nielsen [12] reported a case in which two pits were present, and Stood [13] reported a case in which the condition was bilateral. The depth of these pits varies from a just appreciable amount to as much as 8 to 9 mm. The vision is usually unaffected but may be greatly reduced (fig. 6).

Pathologic examinations of these holes have been made by Coats,[14] Lauber,[15] Rochat,[16] Seefelder [17] and Calhoun.[18] They all agree as to the essential features. These craters are cystic defects in the mass of nerve tissue behind the level of the papilla. The cavity contains "rudimentary retinal tissue associated with irregular glial elements which, dipping down into the intermediary tissue near the point of junction of the lamina cribrosa with the scleral promontory, extends downward toward the vaginal sheath and carries into relation with its inner aspect." In Coats's [14] and Calhoun's [18] cases there was some pigmentation present. In Calhoun's case the pit was associated with a coloboma of the nerve.

Lauber [15] and Seefelder [17] expressed the belief that these pits or craters are rudimentary colobomas.

Vessels on the Disk.—The central artery and vein emerge at the center of the disk and divide into the upper and lower papillary branches on or near the disk, and these in turn divide into the upper nasal and upper temporal and lower nasal and lower temporal branches of the retinal vessels. The central artery and its branches on the disk lie to

11. Stock, W., and von Szily, A.: Klin. Monatsbl. f. Augenh. **44**:48, 1908.
12. Nielsen, J.: Acta ophth. **2**:291, 1924.
13. Stood, W.: Klin. Monatsbl. f. Augenh. **22**:285, 1884.
14. Coats, G.: Roy. London Ophth. Hosp. Rep. **17**:178, 1908.
15. Lauber, T.: Ztschr. f. Augenh. **22**:494, 1909.
16. Rochat, G.: Klin. Monatsbl. f. Augenh. **16**:444, 1913.
17. Seefelder, R.: Arch. f. Ophth. **90**:129, 1915.
18. Calhoun, F. C.: Bilateral Coloboma of Optic Nerve Associated with Holes in Disk and Cyst of Optic Sheath, Arch. Ophth. **3**:78 (Jan.) 1930.

the nasal side of the vein and its branches. Macular vessels branch off from the vessels on the disk and go over the temporal border to surround the macula.

The normal relation of the arteries and veins is 2:3 or 3:4. The veins are increased in size in the presence of inflammation, while the arteries are diminished or irregular in cases of arteriosclerosis, spasm or quinine intoxication.

Normally the arteries are lighter in color than the veins. The veins, however, become lighter in cases of leukemia, lipemia and anemia. In cases of intoxications, cyanosis retinae and polycythemia the veins may become very dark.

The arteries have a reflex or light streak in the center under normal conditions. This is rarely present in the veins. Loss of this light reflex may be an important sign of beginning swelling of the disk, as slight edema may cause this sign.

Irregularities may be present in the vessels. The veins usually cross under (or behind) the arteries. Arteriosclerosis and vascular hypertension (spasm) cause irregularities in the arteries. The veins are often irregular at an arteriovenous crossing where an arteriosclerotic artery causes compression.

Pulsation of the veins on the disk is a common physiologic phenomenon, seen most often just as the veins disappear at the edge of the physiologic cup. Arterial pulsation is always pathologic and has been noted in cases of glaucoma, arteriosclerosis, valvular disease, aneurysm of the aorta, exophthalmic goiter, general anemia and imminent syncope. It occurs most frequently in cases of glaucoma and is not an important sign. No diagnosis, local or general, is made from arterial pulsation alone.

Some of the anomalies of the vessels are described.

Cilioretinal Arteries: These arteries are present in 10 per cent of all eyes. They appear from the edge of the disk, usually on the temporal side, and go to the retina as a small macular branch. An aberrant branch of the central retinal artery may have the appearance of a cilioretinal artery. If the vessel loops at the margin of the disk it is usually a cilioretinal artery. While these are usually small vessels, they may be large and extend well beyond the macula (Wilmer [19]). According to Elschnig [20] and E. Fuchs,[21] they usually arise from the vascular circle of Zinn (fig. 7).

In embolism of the central retinal artery the presence of a cilioretinal artery may result in the sparing of the macula.

19. Wilmer,[1] plate 4.
20. Elschnig, A.: Arch. f. Ophth. **44**:144, 1897.
21. Fuchs, E.: Klin. Monatsbl. f. Augenh. **71**:583, 1923.

The anomaly is usually congenital but may be newly formed after embolism of the central retinal artery.

Cilioretinal Vein: There being no venous circle of Zinn, cilioretinal veins are rare. When this condition does occur the vein may be so large that most of the return blood flows through it. Kraupa [22] has called this anomaly a disk marginal vein.

Opticociliary Vein (Opticochoroidal; Kraupa [22]): This vein draws blood from the central retinal vein into the choroidal circulation. According to Höeg [23] the condition is rare and may follow choked disk or glaucoma.

Fig. 7.—Cilioretinal artery. (From Wilmer,[1] plate 4.)

Opticociliary Arteries: These are extremely rare, and according to Kraupa [22] they have been reported only 3 times.

Prepapillary Arterial Loop: This condition was first described by Liebreich [24] in 1871 as an aberrant retinal vessel in the human vitreous, and since that time it has been reported less than 40 times. Kipp [25] at first regarded the condition as a persistent hyaloid artery.

The anomaly consists of an arterial loop which extends into the vitreous. It may twist around itself "as the snake in the caduceus

22. Kraupa, E.: Arch. f. Augenh. **78**:182, 1915.
23. Höeg, N.: Arch. f. Ophth. **55**:256, 1903.
24. Liebreich, R.: Tr. Path. Soc. London **22**:221, 1871.
25. Kipp, C. J.: Arch. f. Augen- u. Ohrenh. **3**:190, 1874.

twines around the staff," or it may assume other forms from a simple loop to a large loop containing several small ones. Merrill and Wagener [26] in a review of the literature found that a similar venous anomaly was rare. It has been established that the condition is merely a preretinal loop in the retinal circulation. Goldstein and Wexler,[27] as a result of their microscopic study of one of these loops, concluded that there is no membrane or sheath in intimate contact with the vessel and that no structure, unless it is the vitreous, is demonstrated. They also concluded that the loop does not carry with it into the vitreous any elements derived from the retina (fig. 8).

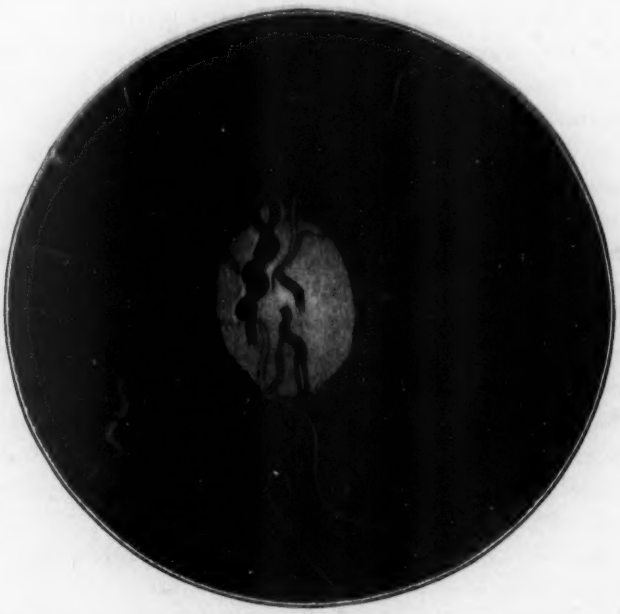

Fig. 8.—Prepapillary arterial loop. (From Wilmer,[1] plate 15.)

Racemose Arteriovenous Aneurysm: This condition is a characteristic anomaly of the papilloretinal vessel. It consists of a direct communication between an artery and a vein, with marked dilatation and tortuosity of both, the venous side usually being affected more than the arterial. Cases have been described by Magnus,[28] Gunn,[29] Schleich,[30]

26. Merrill, V. H., and Wagener, H. P.: Am. J. Ophth. **7**:177, 1924.

27. Goldstein, I., and Wexler, D.: Preretinal Artery: An Anatomic Study, Arch. Ophth. **1**:324 (March) 1929.

28. Magnus, H.: Virchows Arch. f. path. Anat. **60**:38, 1874.

29. Gunn, M.: Tr. Ophth. Soc. U. Kingdom **4**:156, 1884.

30. Schleich, G.: Mitt. a. d. ophth. Klin. in Tübingen **2**:202, 1884.

Seydel,[31] Ehlers,[32] Rentz [33] and Stokes.[34] According to Duke-Elder,[35] the case reported by Kreutz [36] is rather doubtful, so that there have been only 7 authentic cases described in the literature. With the exception of Gunn's case, the vessels of the aneurysm were all markedly dilated. The condition is usually considered congenital, although Magnus stated that trauma is a factor. Leber [37] and Stokes, however, expressed the belief that the anomaly existed in Magnus' case prior to the injury, an opinion that appears to be confirmed when the case history is studied.

Angiomatosis Retinae (Von Hippel's Disease): Angiomatosis retinae is included because of the similarity in appearance of the vessels in the early stage. Here the artery and vein are markedly enlarged but connect with a berry-like reddish mass in the periphery. There is no confusion in the later stages, when exudate, detachment of the retina and gliosis are present.

The condition was first described by von Hippel [38] in 1904, but it was not until 1927 that Lindau [39] demonstrated that the condition is part of an angiomatosis of the central nervous system. The disease has a familial tendency and is accompanied by cerebellar, pancreatic and renal cysts. Twenty-five per cent of the patients die due to cerebrellar cysts.

Level of the Disk.—The normal disk appears to be flush with the rest of the fundus except for the physiologic cup. With the binocular ophthalmoscope, however, it is apparent that there is a slight elevation at the edge of the disk.

Abnormal Elevation of the Disk: This condition is seen in cases of inflammation of the disk or the surrounding retina or in cases of retinal disease. In addition, there may be 6 or more diopters of elevation in cases of choked disk.

Excavations of the Disk: There are three types of excavations: physiologic, pathologic and congenital.

The physiologic cup results embryologically from atrophy of Bergmeister's primitive epithelial papilla with atrophy of the hyaloid artery. The absence of medullated nerve fibers beyond the lamina cribrosa is an additional factor.

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31. Seydel, G.: Arch. f. Augenh. **38**:157, 1898-1899.
32. Ehlers, H.: Acta ophth. **2**:374, 1924.
33. Rentz, W.: Arch. f. Augenh. **95**:84, 1925.
34. Stokes, W. H.: Racemose Arteriovenous Aneurysm of the Retina, Arch. Ophth. **11**:956 (June) 1934.
35. Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 2, p. 1388.
36. Kreutz, A.: Wien. med. Wchnschr. **53**:1725, 1903.
37. Leber, T., in von Graefe, A., and Saemisch, T.: Handbuch der gesamten Augenheilkunde, ed. 3, Leipzig, W. Engelmann, 1915, vol. 7, pt. 1, p. 37.
38. von Hippel, E.: Arch. f. Ophth. **59**:82, 1904.
39. Lindau, A.: Acta ophth. **4**:193, 1927.

There are four different types of physiologic cup: a small funnel-shaped cup; a large laterally placed cup; a central basin-shaped or slightly undermined type, which may be very large, and the eccentric, lateral or lateral sloping type. The lamina cribrosa is visible only in the larger and deeper cups. The physiologic cup is never a complete one, there being always a narrow rim of nerve tissue remaining. Edema or inflammation obliterate the cup.

Under the pathologic type of excavation are the atrophic and the glaucomatous cup.

The atrophic cup occurs in association with primary atrophy of the optic nerve. It is always shallow, and the vessels are never lost. It may extend to the margin of the disk, but it approaches it with a gradual slope. Jean [40] stated that the atrophic cup occurs only in eyes that had a large physiologic cup before the atrophy of the optic nerve occurred. The edges of the deep physiologic cup are rounded off, as it were, by the atrophy of the fibers.

The glaucomatous cup is so well known that little will be said regarding it. In the early stages it may be merely a large physiologic cup. For this reason careful plotting of the visual fields and determination of the tension are always indicated in the presence of such a cup.

The typical picture is one in which the cup reaches to the edge of the disk, with an undermining and dipping under of the vessels, often with an apparent break in them. This is accompanied by atrophy of the nerve with the resultant visibility of the lamina cribrosa. It is essential to remember that the glaucomatous cup may vary between the large physiologic cup and the so-called typical glaucomatous cup (fig. 9).

Two types of pseudoglaucomatous cup may be present.

There may be a large atrophic cup due to a preexisting abnormally large physiologic cup on which atrophy has been superimposed. It is not as deep as the glaucomatous cup. This is illustrated by one of Wilmer's [41] cases. De Schweinitz [42] described a case in which the picture was superimposed on a coloboma of the optic nerve. (fig. 10).

There may be a congenital excavation in which there is a deep cup extending to the margins of the disk with undermining present. A normal nerve with its normal arrangement of vessels is visible at the bottom of a pit in the surrounding tunics. The edge of the excavation is sharp and is surrounded by a halo of atrophic and pigmented choroid exposing the bare sclera. Kayser,[43] Young [44] and others expressed the

40. Jean, G. W.: Ophthalmoscopic Diagnosis, New York, E. B. Meyrowitz, 1915, p. 49.

41. Wilmer,[1] plate 22.

42. de Schweinitz, G.: Ophth. Rec. **20**:384, 1911.

43. Kayser, B.: Klin. Monatsbl. f. Augenh. **45**:76, 1907.

44. Young, T.: Tr. Ophth. Soc. U. Kingdom **45**:267, 1925.

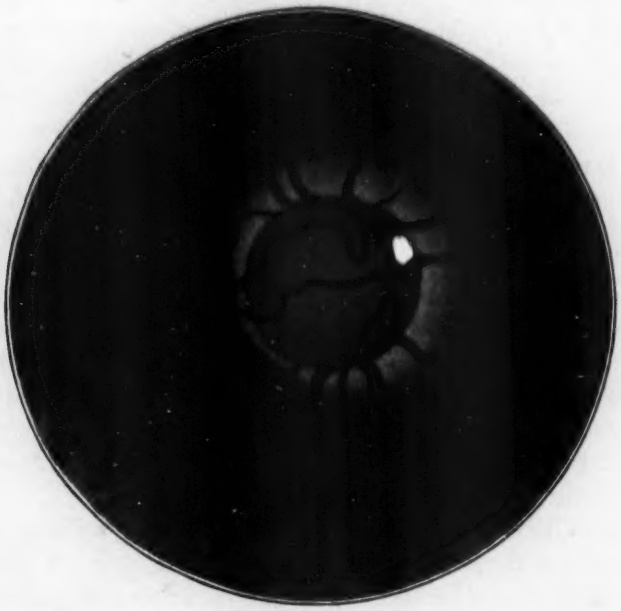

Fig. 9.—Glaucomatous cup. (From Wilmer,[1] plate 24.)

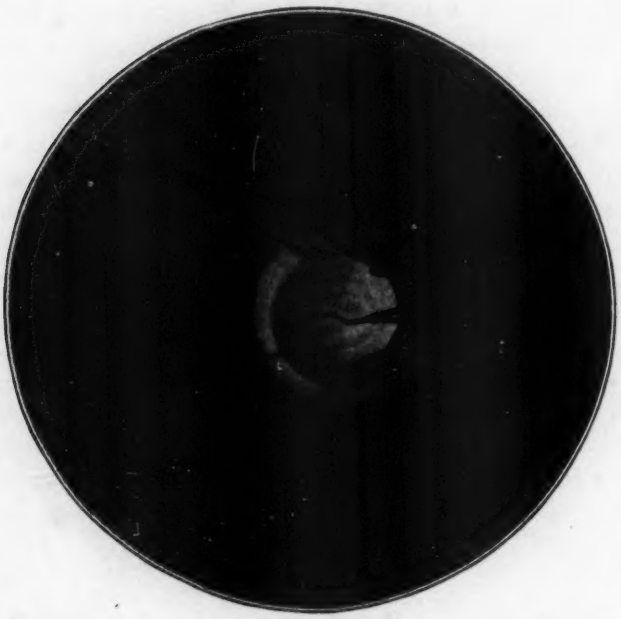

Fig. 10.—Pseudoglaucomatous cup (atrophy of Leber's disease). (From Wilmer,[1] plate 22.)

belief that this is not a coloboma since there is no actual defect, but that it seems rather to be in the nature of an ectasia of the ocular tunics.

Other Congenital Anomalies of the Disk.—Pigment Spots on the Disk: These may occur in varying amounts and may cover the disk. They are of no practical importance, and, according to Ogawa,[45] Bourquin [46] and others, they may be congenital or may follow hemorrhage.

Medullated Nerve Fibers: These nerve fibers usually appear in the retina adjacent to the disk. They consist of flame-shaped, shining white areas with a definite feather edge. At times they may appear

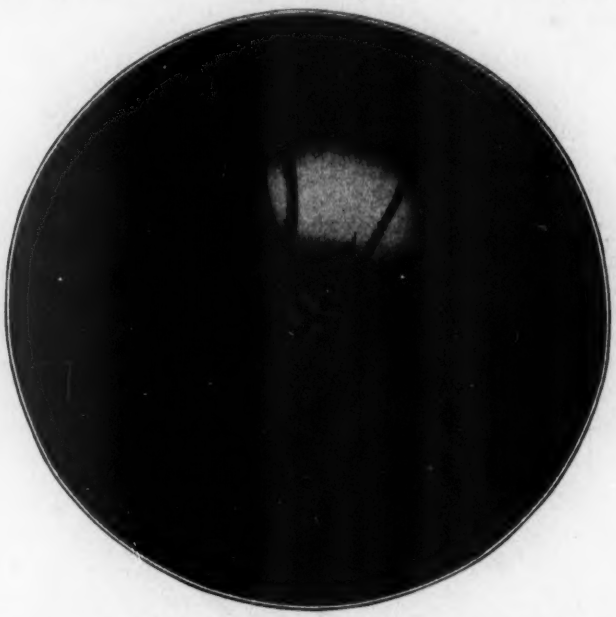

Fig. 11.—Medullated nerve fibers. (From Wilmer,[1] plate 14.)

on the disk in small patches, as described by Szántó,[47] or, as in Blascheck's [48] case, they may cover the entire disk. At times a small, isolated, flame-shaped, feathered-edge patch may be found in the mid-periphery of the retina. These areas on the disk and in the retina are due to failure of the optic nerve fibers to lose their myelin sheaths as they pass through the lamina cribrosa. Berliner [49] has suggested that they are due to the abnormal presence of myelin-forming elements in the layer of nerve fibers (fig. 11).

45. Ogawa, K.: Arch. f. Augenh. **52**:437, 1905.
46. Bourquin, J.: Ztschr. f. Augenh. **37**:166, 1917.
47. Palich Szántó, O.: Klin. Monatsbl. f. Augenh. **55**:149, 1915.
48. Blascheck, A.: Ztschr. f. Augenh. **9**:428, 1903.
49. Berliner, M. L.: Cytologic Studies on Retina: Normal Coexistence of Oligodendroglia and Myelinated Nerve Fibers, Arch. Ophth. **6**:404 (Sept.) 1931.

Persistent Hyaloid Artery: This artery appears as a fibrous band protruding from the disk into the vitreous. At times a portion of it near the disk may remain filled with blood, which can be seen pulsating rhythmically with the heart. Koller [50] described a case in which the artery assumed cystlike proportions on the disk. The condition is due to failure of the hyaloid artery to atrophy and is frequently associated with amblyopia.

Cloquet's Canal: The aforementioned type of persistent hyaloid artery is the so-called true persistent hyaloid artery. A second type is a hollow, trumpet-shaped tube, free from blood, known as Cloquet's canal. Its distal end is affixed to the lens capsule and is known as the campanula Halleri.

Persistent Falciform Ligament: There is a third form in which the disk is covered by a dazzling white conical mass of fibrous tissue, which terminates in a strong white fibrous cord split into three smaller cords, which can be traced to the sides and center of the lens capsule. This falciform ligament occurs normally in fish. Johnson and Head [51] have an excellent example in their book.

Membrana Epipapillaris: This is a fibrous membrane on the optic disk which is often combined with white sheaths around the vessels. According to Botteri,[52] they may be so dense that they obscure the vessels. Others, however, arise from the disk and appear as a delicate veil-like structure with slightly curled edges, probably of neuroglial origin. This subject has been thoroughly reviewed by Samuels [53] (fig. 12).

Drusen on the Disk: These are hyaline bodies on the disk. In approximately one third of the cases they produce no symptoms or interference with vision. They may be distributed variously—surrounding the vessels, at the edge of the disk or over the entire disk. They are one to two vein diameters in size, round and shining white in appearance. They are often congenital but may be associated with retinitis pigmentosa, choked disk, optic neuritis and atrophy of the optic nerve. These drusen have been regarded as a separate entity not to be confused with corpora amylacea. According to Lauber,[54] they have a familial tendency (fig. 13).

Congenital Absence of the Optic Nerve, Hypoplasia, Aplasia and Misplacement: These are rare conditions which are found in congenitally abnormal eyes.

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50. Koller, C.: Tr. Am. Ophth. Soc. **9**:380, 1911.
51. Johnson and Head,[2] plate 3, fig. 6.
52. Botteri, A.: Klin. Monatsbl. f. Augenh. **48**:11, 1910.
53. Samuels, B.: Tr. Am. Ophth. Soc. **29**:242, 1931.
54. Lauber, T.: Ztschr. f. Augenh. **17**:391, 1907.

Fig. 12.—Membrana epipapillaris. (From Wilmer,[1] plate 16.)

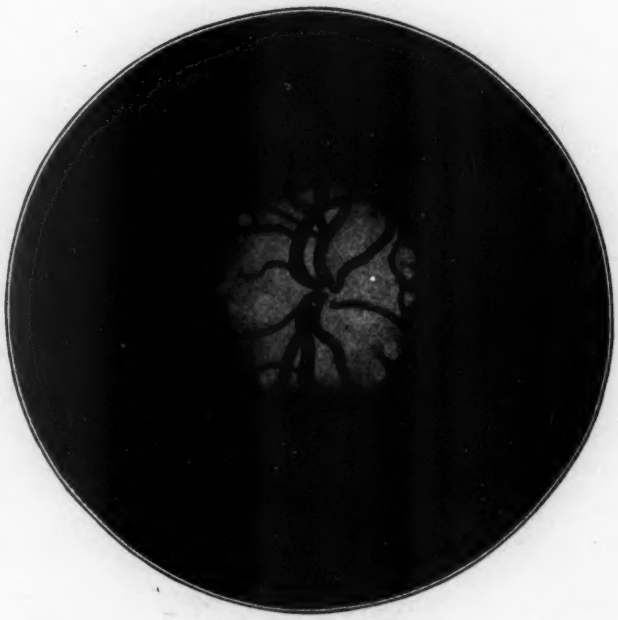

Fig. 13.—Drusen on the disk. (From Wilmer,[1] plate 35.)

Pseudoneuritis: This is a congenital condition that resembles optic neuritis. The primary deformity is probably ectodermal, depending on neuroglial overgrowth. The disk is swollen up to 10 diopters, is hyperemic and at times is dirty gray, with the margin of the disk striated and ill defined. The vessels are normal in caliber and can be followed as they curve from the swollen disk to the retina. The anomaly is distinguished from a pathologic condition by the fact that it is congenital and nonprogressive, that there are no hemorrhages or exudates present and that the vessels are normal. It occurs almost invariably in small hypermetropic eyes in which astigmatism is usually present. However, according to Heine,[55] it has also been noted in association with emmetropia and myopia. The visual acuity is usually below normal.

The condition may occur familially, when it is known as congenital familial pseudoneuritis. Lambert and McDannald [56] reported its occurrence in 4 members of a family, while it occurred in 6 sisters of a family reported by Heine.[55] Nottbeck [57] reported 15 cases, 12 of the patients being under 20 years of age. Therefore it is necessary to be extremely cautious in making a diagnosis of pseudoneuritis as the result of a single examination. As Bartels [58] has pointed out, it is in this young group that one is often called on to decide from the fundus examination whether or not there are complications referable to the brain as the result of acute disease of the middle ear.

INJURIES TO THE OPTIC DISK

Evulsio Nervi Optici.—Salzmann [59] gave this name to a condition in which the optic nerve together with the lamina cribrosa is torn out of the scleral hole. About 25 cases have been reported, and probably many more have been overlooked because of extensive intraocular hemorrhage. Ophthalmoscopically, the picture is recognized by an absence of the disk and its vessels. In the later stages the vessels of the retina may also entirely disappear. Weinstein [60] reported a case in which the injury was bilateral and in which, because of the hemorrhage, it was not possible to determine the lesion in one eye until some time after the accident.

According to Rönne,[61] 50 per cent of the injuries were caused by a thin rodlike foreign body, such as the tip of an umbrella, entering the

55. Heine, L.: Arch. f. Ophth. **102**:339, 1920.
56. Lambert, R. K., and McDannald, C. E.: Am. J. Ophth. **14**:46, 1931.
57. Nottbeck, B.: Arch. f. Ophth. **44**:31, 1897.
58. Bartels, M.: Ztschr. f. Augenh. **21**:231, 1909.
59. Salzmann, M.: Ztschr. f. Augenh. **9**:489, 1903.
60. Weinstein, A.: Klin. Monatsbl. f. Augenh. **46**:531, 1908.
61. Rönne, H., in Schieck, F., and Brückner, A.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1930, vol. 5, p. 633.

orbit alongside the optic nerve. Most of the remainder were due to gunshot wounds in the temporal region. Extensive chorioretinal changes frequently occur in these cases.

Oblique Injuries.—These injuries, called by Goldzieher [62] chorioretinitis plastica sclupetaria, are ones in which the nerve is severed directly behind the eyeball. Ophthalmoscopically, the picture is one of complete primary atrophy of the optic nerve with extensive chorioretinal changes. Most of the injuries result from gunshot wounds in the temporal region in attempted suicide. Würdemann [63] reported such a condition due to a war injury; after two years the media were still clear and the eyeball was normal in appearance. Lister [64] also described this condition occurring as a result of war injuries.

Direct Injuries to the Disk.—Foreign bodies may also produce direct injuries. Lauber [65] collected 23 such cases, in 11 of which the diagnosis was made by ophthalmoscopic examination. The degree of damage depends on the size of the foreign body, its location, the material and the reaction of the eye. The foreign body may sever the central vessels with complete loss of vision. If the foreign body is superficial, it may not cause any damage to vision or it may cause a sector-like field defect. If the foreign body is iron and siderosis develops, the eye is lost.

TUMORS OF THE OPTIC DISK

Primary Tumor.—This type of tumor is very rare but has been observed microscopically a number of times. von Michel [66] reported a fibroma arising from the connective tissue of the hilus of the disk. The growth in Schieck's [67] case was diagnosed as a perithelioma, arising from the peripheral cells of the vessels. Sidler-Huguenin [68] reported an endothelioma, while sarcomas have been reported by Oloff,[69] Vasquez-Barrière [70] and Speciale-Cirincione.[71] The tumors appear to be primarily benign in type.

Secondary Tumor.—The secondary tumor occurs either by direct extension or by metastatis. Retinoblastoma, sarcoma and carcinoma have been reported.

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62. Goldzieher, W.: Ztschr. f. Augenh. **6**:277, 1901.
63. Würdemann, H.: Am. J. Ophth. **6**:842, 1923.
64. Lister, W. T.: Brit. J. Ophth. **8**:305, 1924.
65. Lauber, T.: Ztschr. f. Augenh. **32**:360, 1914.
66. von Michel, J.: Ztschr. f. Augenh. **13**:68, 1905.
67. Schieck, F.: Arch. f. Ophth. **81**:328, 1912.
68. Sidler-Huguenin: Arch. f. Ophth. **101**:113, 1920.
69. Oloff, H.: Klin. Monatsbl. f. Augenh. **55**:313, 1915.
70. Vasquez-Barrière, A.: Klin. Monatsbl. f. Augenh. **49**:43, 1911.
71. Speciale-Cirincione: Ann. di ottal. e clin. ocul. **53**:9, 1925.

Gumma of the Disk.—This type of growth is rather rare and has been reported only a relatively few times. In Juler's [72] case the papilla was swollen and resembled a tumor. Microscopically, there was an intense leukocytic inflammation of the nerve, retina and choroid, with some hemorrhage into the retina, principally in the nerve fiber layer. Parsons [73] reported a case in which he found similar changes but with necrosis of the nerve head.

The usual picture, according to Mylius,[74] is that of a choked disk, often accompanied by opacities of the vitreous.

It has been stated that the prognosis in these cases is poor, even though energetic antisyphilitic treatment is employed.

TUBERCULOSIS OF THE DISK

The one tuberculous lesion of the disk that is characteristic is the solitary tubercle of the disk. This has been described by Knapp,[75] Weiss,[76] Coats,[77] Komoto [78] and others. The lesion consists of an ill defined, white mass, situated on the center of the disk or near its margin, that protrudes into the vitreous. In the early stages it may cause no loss of function, but later a sector-like bundle field defect develops. The prognosis in these cases is poor, as most of the eyes are lost due to keratitis and secondary glaucoma.

Another type of tuberculosis, described among others by A. Knapp [79] and Friedenwald,[80] that resembles the solitary tubercle of the disk is the lesion found at the margin of the disk but situated primarily in the retina. The prognosis is much better for this type.

DISEASES OF THE OPTIC DISK

The discussion here will be limited to the ophthalmoscopic picture of the diseases of the optic nerve.

Papilledema (Choked Disk).—Because of absence of early symptoms, choked disk is rarely seen in the earliest stages. Therefore, there is still some controversy regarding the earliest appearance of swelling.

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72. Juler, F.: Arch. d'opht. **17**:542, 1897.
73. Parsons, J. H.: The Pathology of the Eye, New York, G. P. Putnam's Sons, 1905, vol. 2, p. 683.
74. Mylius, K.: Klin. Monatsbl. f. Augenh. **51**:648, 1913.
75. Knapp, A.: Arch. Ophth. **32**:22, 1903.
76. Weiss, L.: Arch. f. Ophth. **23**:4, 1877.
77. Coats, G.: Roy. London Ophth. Hosp. Rep. **16**:381, 1905.
78. Komoto, J.: Klin. Monatsbl. f. Augenh. **50** (pt. 1):82, 1912.
79. Knapp, A.: Arch. f. Augenh. **75**:259, 1913.
80. Friedenwald, J.: Tr. Am. Ophth. Soc. **9**:577, 1902.

Schieck,[81] Meesmann [82] and Koeppe [83] stated that the first sign as seen by the slit lamp (with the aid of a contact glass) is a veiling of the center of the disk, resulting from a detachment of the internal limiting membrane. This is accompanied by a filling of the perivascular lymph spaces of the central vessels. Ophthalmoscopically, this produces a definite white line along the central vessels. This is followed by a fine striped, washed-out appearance of the disk and retina, surrounding the vessels, that finally covers the entire disk.

According to Paton and Holmes [84] and others, choked disk begins with a swelling of the nerve fiber sheaths in a limited area of the disk, usually above and never at first at the temporal side. The vessels of the disk then are elevated by the edema, that spreads to all sides. The optic cup is spread at first and remains visible for a long time as a slitlike funnel.

There is no controversy regarding the later stages. As the disk becomes more congested, there is less contrast between it and the surrounding retina. The disk tissue becomes more and more opaque and fine radiating striations appear, so that the margin of the disk becomes obliterated. As the edema spreads to the surrounding area, the typical elevation of the disk, usually mushroom-like or champagne cork-like (fig. 14), appears. This is visible ophthalmoscopically by the curve of the vessels and the difference of refraction between the disk and the surrounding retina. There may be a difference of 6 to 7 diopters. The edema that obliterates the normal margin of the disk makes the disk appear twice its normal size. Occasionally this false margin is emphasized by the appearance of white stripes at its edge, resulting from circumpapillary folding of the retina (fig. 15).

The arteries are contracted and more or less hidden in the congested edematous tissue, and the superficial ones are in part covered by a veil. The veins are dilated, tortuous and filled with dark blood.

Frequently there are present on the disk, small white, glistening points of exudate or somewhat larger, grayish red areas of exudate. Small hemorrhages are present that later may form a hemorrhagic wreath surrounding the disk. There are also not infrequently patches of exudate between the disk and the macula. Typical stellate figures have been described a number of times. Paton [85] found this stellate figure twenty-two times in a series of 146 cases of choked disk.

In the acute type there is a good deal of edema, hemorrhage and exudate, while in the more slowly developing type there are less edema,

81. Schieck, F.: Arch. f. Ophth. **78**:1, 1911.
82. Meesmann, A.: Klin. Monatsbl. f. Augenh. **66**:417, 1921.
83. Koeppe, L.: Arch. f. Ophth. **109**:454, 1922.
84. Paton, L., and Holmes, G.: Brain **33**:389, 1911.
85. Paton, L.: Brain **32**:65, 1909.

Fig. 14.—Early choked disk. (From Wilmer,[1] plate 27.)

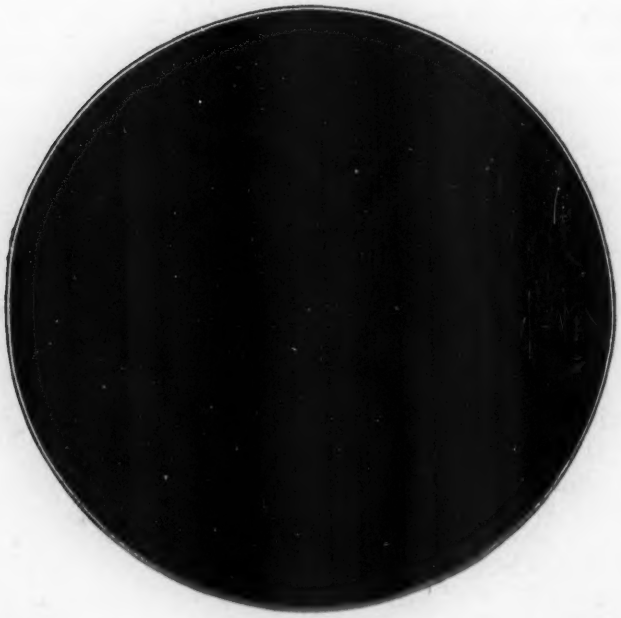

Fig. 15.—Advanced choked disk. (From Wilmer,[1] plate 28.)

less hemorrhage and an apparent increase of small vessels on the disk, the latter resulting from a dilation of the capillaries.

Without doubt the fully developed choked disk can recede without leaving visible evidence of its existence. If the papilledema has persisted for a time, atrophy of the optic nerve sets in. As the swelling subsides, the disk assumes a grayish color that gradually changes into a typical secondary atrophy of the optic nerve. The margin of the disk is no longer cleancut, and there is some disturbance in the pigmentation. The tortuosity of the veins and the contraction of the arteries may persist. Drusen may develop on the disk following papilledema.

Choked disk is almost always bilateral. The degree of swelling in the two eyes and the first eye involved have no relation to the site of the tumor.

Papillitis (Optic Neuritis).—Papillitis is an inflammation of the optic nerve that must be differentiated from choked disk. It results from foci of inflammation in the optic nerve itself and as a rule produces early interference with vision in the central field. The etiologic factors are numerous.

Ophthalmoscopically, the margin of the disk is blurred due to edema; there is dilatation of the veins with a slight contraction of the arteries, and the disk is hyperemic due to dilatation of the capillaries. Exudates and hemorrhages are present in varying degrees, depending on the severity of the disease. In many cases the retina is also involved, producing neuroretinitis. The swelling is rarely over 2 diopters, and the inflammation is usually unilateral. In certain cases, especially in cases of syphilis, opacities of the vitreous develop (fig. 16).

Papillitis may disappear, leaving no evidence of the disease or at most a small amount of exudate on the disk and along the vessels. In the severer types that persist or are the result of a toxic condition, atrophy of the optic nerve of the secondary type develops.

The differential diagnosis between optic neuritis and early choked disk is often difficult and in many instances cannot be made from the fundus picture alone. A cloudiness of the posterior part of the vitreous is often present in cases of optic neuritis but never in cases of choked disk. Another factor of considerable importance is that optic neuritis is usually unilateral, while choked disk, with a few exceptions, is always bilateral. The swelling of the disk is rarely over 2 diopters in cases of optic neuritis, while it often goes to 6 or 7 diopters in cases of papilledema. Central vision is usually involved early in optic neuritis.

Examination of the perimetric and central fields and general physical and neurologic examinations are necessary in many cases before a final diagnosis can be made.

Retrobulbar Neuritis.—Retrobulbar neuritis is a disease of the retrobulbar portion of the optic nerve. It may be acute or chronic, is due to multiple factors and has as its most common diagnostic finding central or pericentral scotomas. It has been stated that the condition in 33 per cent of the cases is due to multiple sclerosis.

Clinically, the disease has been divided into several types: (*a*) acute axial optic neuritis; (*b*) chronic axial optic neuritis (toxic amblyopia); (*c*) demyelinating optic neuritis, and (*d*) hereditary atrophy of the optic nerve (Leber's disease). The disease is so complex that only a résumé of the ophthalmoscopic findings of the group as a whole will be given.

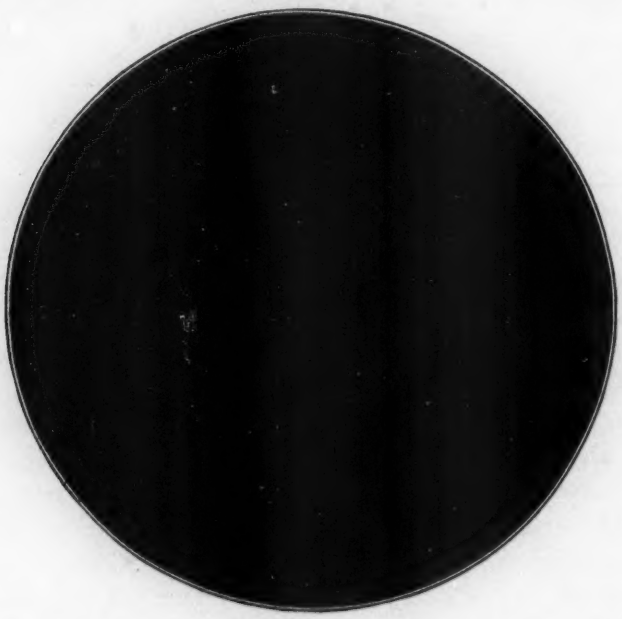

Fig. 16.—Mild optic neuritis. (From Wilmer,[1] plate 34.)

Ophthalmoscopically, the disk may be normal, especially when the condition develops early or is transient. Often there is a slight veiling and a little cloudiness of the disk. When the disease is chronic or more severe the disk develops the typical temporal atrophy. Certain types may produce a mild optic neuritis. In Leber's disease, as the condition progresses a mild optic neuritis develops that gradually changes to a yellow gray atrophy involving the entire disk. The temporal half as a rule shows more involvement than the remainder of the disk.

Atrophy of the Optic Nerve.—Ophthalmoscopically, several types of atrophy of the optic nerve may be distinguished.

Retinal or Yellow Atrophy: This type is one in which the disk has a pale yellowish color, that has also been described as waxy. The retinal

vessels show a marked contraction. The condition is secondary to retinal disease and is seen in the typical form in well advanced retinitis pigmentosa (fig. 17).

Primary Atrophy: This type results from disease or severance of the optic nerve behind the disk. The typical disk is a translucent white. In cases of tabes the disk may have a bluish gray mottled appearance, the so-called gray atrophy of tabes. In primary atrophy the margin of the disk is sharply defined and distinct. There is a shallow atrophic cup present that begins at the margin of the disk, in which the lamina cribrosa is clearly visible. The vessels are normal in size in most

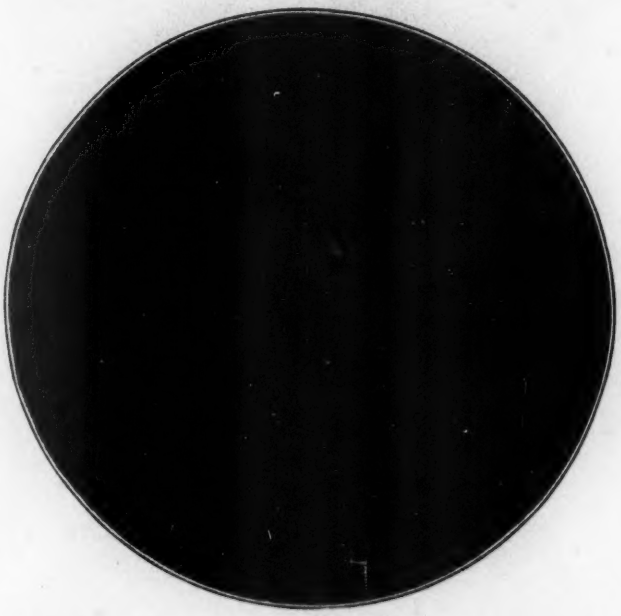

Fig. 17.—Retinal (yellow) atrophy after retinitis pigmentosa. (From Wilmer,[1] plate 78.)

instances, but at times they are slightly smaller in caliber and devoid of all their fine branches. It is important to remember that primary atrophy may be superimposed on old mild postneuritic changes (fig. 18).

Secondary (Postneuritic) Atrophy: This type follows severe inflammation of the disk. The disk is white (chalky white), with a blurred or obliterated margin. The vessels are contracted, with some white streaks along their sides. The optic cup is filled with connective tissue. It is this connective tissue which is left after the neuritic exudate that causes the intense white color, the blurred edges and the streaks along the vessels (fig. 19).

Fig. 18.—Primary atrophy of the optic nerve. (From Wilmer,[1] plate 20.)

Fig. 19.—Secondary atrophy of the optic nerve. (From Wilmer,[1] plate 21.)

Glaucomatous Atrophy: This type of atrophy is readily recognized because of the presence of the glaucomatous cup.

Temporal Atrophy of Retrobulbar Neuritis: This type of atrophy has already been discussed.

Vascular Atrophy: Closing off the blood supply in the central retinal artery gives rise to this type of atrophy. It is seen in association with embolism of the central retinal artery and quinine poisoning. The vessels show a marked contraction or obliteration. Aside from this, the picture is that of primary atrophy.

NOTE.—In this review relatively little space has been devoted to the diseases of the papilla because it was felt that these are better understood than are the congenital anomalies of the optic disk.

Correspondence

PUPILLARY RESPONSE TO PHYSOSTIGMINE SALICYLATE IN ABSENCE OF OCULOMOTOR NERVE

To the Editor:—I was surprised on reading Spiegel and Scala's "Role of the Cervical Sympathetic Nerve in the Light Reflex of the Pupil" in the February issue of the ARCHIVES, page 371, to note that they were able to obtain contraction of the pupil of an eye deprived of its oculomotor nerve by instilling physostigmine salicylate (protocol, page 373).

Although I have never had the opportunity to observe the action of this drug on the pupil of an eye deprived of its third nerve, both Duke-Elder (Text Book of Ophthalmology, London, Henry Kimpton, 1932, vol. 1, p. 545) and Berens (The Eye and Its Diseases, Philadelphia, W. B. Saunders Company, 1936, p. 949) state that it has no miotic action if oculomotor impulses are not effective. Their explanation is that physostigmine salicylate is not a stimulant in itself but activates the oculomotor end apparatus by inhibiting the destruction of acetylcholine by the enzyme choline-esterase, so that the acetylcholine may maintain its effectivity over a long period.

I should appreciate any light that might be shed on this apparent discrepancy.

PAUL T. MCALPINE, M.D., New York.

To the Editor:—The loss of the response of the pupil to physostigmine salicylate does not develop immediately after severance of the oculomotor nerve but within a few days after the operation. As pointed out by Sollmann (A Manual of Pharmacology, ed. 5, Philadelphia, W. B. Saunders Company, 1936, p. 345), it seems that the loss of the miotic response is related to the development of degenerative changes, which requires a certain time. In our experiment the section of the oculomotor nerve and the instillation of physostigmine salicylate were made on the same day, as shown by the protocol (page 373), so that a reaction to the drug could still be obtained.

E. SPIEGEL, M.D., Philadelphia.

Notices

A NEW FEATURE OF THE ARCHIVES

Question and Answer Department.—To enable readers of the ARCHIVES to obtain information, if available, on a problem which has presented itself in their practice, a new department, called Questions and Answers, will be established, under the direction of Dr. W. L. Benedict.

This plan has been carried out with success in one of the European ophthalmic journals and should be of service to the readers of the ARCHIVES.

Questions are to be sent to Dr. W. L. Benedict, the Mayo Clinic, Rochester, Minn., accompanied by the sender's name or, if preferred, initials. The questions and the answers will be published in subsequent numbers of the ARCHIVES.

News and Notes

EDITED BY W. L. BENEDICT

SOCIETY NEWS

Association for Research in Ophthalmology.—The Association for Research in Ophthalmology will hold its eleventh scientific meeting in New York on June 11.

The program for the morning session (9:30) follows:

"Effect of Pressure on Conical Cornea," Dr. T. L. Terry and Dr. Julian F. Chisholm, Massachusetts Eye and Ear Infirmary, Boston.

"Effect of Certain Physical and Chemical Stimuli on the Caliber of the Retinal Vessels in Man," Dr. Irving Puntenney, department of ophthalmology, Northwestern University Medical School, Chicago.

"Some Pharmacological Experiments on Isolated Segments of Mammalian Iris," Dr. Erich Sachs and Dr. Parker Heath, department of ophthalmology, Wayne University, Detroit.

"Passage of Horse Serum from the Blood Stream into the Aqueous Humor of Normal and Immunized Animals," Dr. Loren Guy, department of ophthalmology, Cornell University Medical College, New York.

The program for the afternoon session (2:30) will consist of:

"Cultivation of Conjunctivitis-Producing and Keratitis-Producing Agents on the Chorio-Allantoic Membrane of the Chick Embryo," Dr. Phillips Thygeson, department of ophthalmology of the College of

Physicians and Surgeons, Columbia University and the Institute of Ophthalmology, Presbyterian Hospital, New York.

"A Comparative Study of the Effects of Mecholyl, Doryl, Eserine, Pilocarpine, Atropine and Epinephrine on the Blood-Aqueous Barrier," Dr. Kenneth C. Swan and Mr. William Hart, department of ophthalmology, University of Iowa, Iowa City.

"The Mucopolysaccharide Acid of the Cornea and Its Enzymatic Hydrolysis," Dr. Karl Meyer, and Eleanor Chaffee, department of ophthalmology of the College of Physicians and Surgeons, Columbia University and the Institute of Ophthalmology, Presbyterian Hospital, New York.

"Dark Adaptation of Normal Adults on Diets Deficient in Vitamin A," Dr. Lincoln F. Steffens, Dr. Hugo L. Bair and Dr. Charles Sheard, Mayo Clinic, Rochester, Minn.

College Courses for Preparation of Sight-Saving Teachers and Supervisors.—The National Society for the Prevention of Blindness has announced that it is cooperating with the following colleges and universities in offering, at their 1940 summer sessions, courses for the preparation of teachers and supervisors of sight-saving classes:

Oregon State System of Higher Education, Portland, Ore. An elementary course, June 17 to July 26. Director of the course: Miss Olive S. Peck, Supervisor of Sight-Saving, Cleveland Public Schools, Cleveland.

Wayne University, Detroit. An elementary course, June 24 to August 2 or July 1 to August 9. Director of the course: Miss Margaret M. Soares, Supervisor of Braille and Sight-Saving Classes, Detroit.

State Teachers College, Buffalo. An elementary course, July 1 to August 9. Director of the course: Miss Matie M. Carter, Associate Supervisor, Physically Handicapped Children's Bureau, State Education Department, Albany, N. Y.

University of Minnesota, Minneapolis. An advanced course, June 17 to July 26. Director of the course: Mrs. Winifred Hathaway, Associate Director, National Society for the Prevention of Blindness, 50 West Fiftieth Street, New York.

Details regarding any of these courses may be obtained from the university or college or from the director in charge of the course.

UNIVERSITY NEWS

Summer Graduate Course in Ophthalmology.—The University of Rochester School of Medicine and Dentistry, Rochester, N. Y., will conduct its eleventh annual summer graduate course in ophthalmology beginning Monday, July 29, 1940. The course will cover a period of five days.

Dr. Frederick H. Verhoeff will be the guest of honor. Guest lecturers will be: Dr. Thomas D. Allen, Commander J. C. Adams, Dr. Arthur J. Bedell, Dr. Albert L. Brown, Dr. George H. Cross, Dr. Albert D. Frost, Dr. Peter C. Kronfeld, Dr. Henry P. Wagener and Dr. James W. White.

Resident members of the staff are as follows: Dr. John J. Morton, Dr. Albert C. Snell, Dr. John F. Gipner, Dr. Eldred W. Kennedy, Dr. Macy L. Lerner, Dr. Frank Barber, Dr. Eugene R. Vernou, Dr. Charles T. Sullivan, Dr. Wesley F. Bosworth and Dr. Charles Block.

Nonmedical lecturers will be Scott Sterling, Frederick W. Jobe and S. Edgar Wirt, all of the Bausch and Lomb Optical Company.

The tuition fee for the course will be $40. Further information can be obtained by writing to Dr. John F. Gipner, Strong Memorial Hospital, Rochester, N. Y.

CORRECTION

In the article by Dr. Benjamin Friedman entitled "Acceptance of Weak Cylinders at Paradoxic Axes," in the April issue (ARCH. OPHTH. 23: 720, 1940), "18 degrees" in the last line but one on page 724 should read "180 degrees" and "reversing" in the seventh line from the top of page 726 should read "reducing."

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Conjunctiva

NOTE ON PHLYCTENULAR OPHTHALMIA. JAMES BARRETT, Brit. J. Ophth. **23**: 669 (Oct.) 1939.

Barrett states that tuberculous disease in Victoria, Australia, has been greatly lessened but that phlyctenular disease has declined to a much greater extent. This may be due to better conditions and greater care taken to avoid infection, but it may also be the expression of a biologic process of elimination. Furthermore, if the current view is taken, both tubercle and phlyctenular ophthalmia may be due to malnutrition and may not be directly associated.

Two questions arise: 1. Is the fact that a reaction to tuberculin is obtained in cases of phlyctenular ophthalmia and of other types of ophthalmia a certain indication that the cause of the condition is tuberculous? 2. May not both tubercle and phlyctenular ophthalmia be products of malnutrition?

W. ZENTMAYER.

Cornea and Sclera

KERATOCONJUNCTIVITIS IN HYPOFUNCTION OF THE LACRIMAL GLANDS. U. MEDUNINA, Vestnik oftal. **13**: 655, 1938.

In 1933 Sjögren reported 19 cases of spontaneous "dry," or filiform, keratoconjunctivitis due to a disturbance of lacrimation. Women from 45 to 60 years of age (at the menopause) usually are affected. The characteristic signs are the presence of grayish filamentous secretion and accompanying dryness of the mouth and nasopharynx. Sjögren believes that a chronic systemic infection affects the function of the lacrimal and salivary glands and the glands of the upper respiratory tract, with consequent sclerosis and atrophy.

The occurrence of "Sjögren's syndrome" in a woman aged 28 is reported. Neurologically, there was found a marked depression of the parasympathetic nervous system. General and local therapy did not improve the condition to a great extent, as there were remissions.

O. SITCHEVSKA.

ACUITY OF VISION AND THE CAUSES OF IMPAIRMENT OF VISION IN PATIENTS WITH PAST SYPHILITIC INTERSTITIAL KERATITIS. E. DALSGAARD-NIELSEN, Acta ophth. **17**: 43, 1939.

The author examined 173 patients who had suffered from syphilitic interstitial keratitis and records statistics in regard to their visual acuity. For a large group of these patients, the period of observation averaged twenty-one years. Seventy-five per cent of the eyes of this group showed a visual acuity of from 6/6 to 6/18; 11 per cent, an acuity of from 6/24

to 6/60, and 8 per cent, an acuity of less than 6/60; 6 per cent of the eyes were blind.

Many other figures are recorded, showing the incidence of various corneal changes, iridocyclitis, glaucoma, cataract and choroiditis.

O. P. PERKINS.

General Diseases

RETROBULBAR NEURITIS WITH PELLAGRA IN NIGERIA. D. F. MOORE, J. Trop. Med. **42**: 109 (April) 1939.

Moore discusses a syndrome that occurs extensively in Southern Nigeria. It consists of perlèche, sore tongue and genitalia and retrobulbar neuritis associated with atrophy of the optic nerve. The condition has responded dramatically to treatment with autoclaved yeast products and so is believed to be pellagrinous. It is believed that gari, dried parched manioc, plays an important part in its incidence. The facts which support pellagra as the cause of the syndrome in Southern Nigeria are: 1. Throughout the palm oil belt there is an abundance of cheap edible oil. 2. No single case of xerophthalmia has been seen in Southern Nigeria. 3. There is a great relative shortage of animal and fish protein in Southern Nigeria. (It is in these areas, or under conditions that permit this shortage, that this syndrome is found.) 4. Where gari is eaten to excess in the absence of the protein-productive foods it is shown to have an almost constant relation to the incidence of this syndrome. Gari bears a strong suggestive comparison with "spoiled maize." A nutritional policy, based on the recommendations of the health committee of the League of Nations Health (1937), requires that Nigeria develop local food sources and, when possible, abolish both gari and stockfish as dietary essentials of the people by replacement with other foodstuffs.

J. A. M. A.

Glaucoma

INFILTRATION ANESTHESIA IN A CASE OF ACUTE GLAUCOMA. E. BLANC, Bull. Soc. d'opht. de Paris **51**: 66 (Jan.) 1939.

A boy of 10 years was struck in the right eye by a ball. At the time of injury the pain was slight, but forty-eight hours later, at night, it became severe. There was a massive fresh hemorrhage in the anterior chamber. Good perception and projection of light were maintained. The raised intraocular tension did not respond to miotics during a period of five days. Ten cubic centimeters of a 1 per cent solution of procaine hydrochloride was injected into the stellate ganglion. In a few minutes there was relief from pain and inflammation. The tension was reduced from 80 to 40 mm. of mercury. The hemorrhage absorbed slowly, but vision returned to counting of fingers only. A second injection produced a Horner's syndrome after two or three minutes. Vision returned to one-half, the tension was 18 mm. and the visual field became normal. The report is of a single incident and is to be considered as preliminary. Blanc believes the procedure is useful in ocular therapeutics but should not be recommended as a universal panacea.

L. L. MAYER.

TREPHINING COMBINED WITH CYCLODIALYSIS. K. BERGLER, Klin. Monatsbl. f. Augenh. **102**: 49 (Jan.) 1939.

Bergler devised a modification of Sallmann's combined trephining and cyclodialysis after Heine's method. He employed his modification in 45 cases of glaucoma, the results of which are tabulated. Secondary operation was required in 7 cases, and the tension was regulated in all but 1 case. The glaucoma in 25 cases was simple; in 9, chronic; in 3, acute, and in 8, secondary. The operation is more simple than the classic cyclodialysis. The operative technic and anesthesia of Sallmann were adhered to in the principle. A trephine of 2 mm. was preferred in his recent operations, after one of 1.5 mm. had been used in the first operations. Late infections did not occur. Escape of aqueous humor beneath the conjunctiva, near the conjunctival flap, resembling chemosis, disappeared within eight days, except in 1 case, in which it lasted for eight months. The separation of the ciliary body can be performed with greater ease by means of this operation.

K. L. STOLL.

Hygiene, Sociology, Education and History

THE SCHOOL OPHTHALMIC SERVICE. A. FURNISS, Brit. J. Ophth. **23**: 256 (April) 1939.

This lengthy article does not lend itself to abstracting. It describes in detail the methods employed in the examination and care of the eyes of school children at West Ham, England.

W. ZENTMAYER.

ON DISABLEMENT AND SOCIAL CONDITIONS OF PATIENTS WITH PAST SYPHILITIC INTERSTITIAL KERATITIS. E. DALSGAARD-NIELSEN, Brit. J. Ophth. **23**: 544 (Aug.) 1939.

This article is difficult to abstract satisfactorily as it is largely statistical, the findings being arranged in tables and graphs.

Particular attention was paid to the question whether the disease had caused such a degree of disablement that it has impaired the practical earning capacity of the patient. Seventy-nine per cent of the patients stated themselves that they were perfectly capable of work, while 7 per cent were only partially able to work and 14 per cent were disabled probably to a degree less than one third of working capacity. In the main, these statements have agreed very well with the physician's estimate on the appraisal of the disablement.

The symptoms causing disablement have been impairment of vision, deafness and complications involving the nervous system. By far the most frequent cause of disablement was impairment of vision, as this complaint appeared in 92 per cent of the cases, and it was the only complaint in 72 per cent. Among the pathologic changes in the eye found to be the cause of impairment of vision, corneal opacity was the most frequent, while anomalies of refraction and choroiditis were considerably less frequent, and cataract and bulbar phthisis were even more infrequent.

W. ZENTMAYER.

Instruments

A "PIN" EYE-DROPPER. N. B. HARMAN, Brit. J. Ophth. 23: 212 (March) 1939.

Oily preparations of alkaloids for the treatment of ocular diseases are in many cases preferable to watery solutions. They keep better, and in some cases they are more effective. To avoid messiness from too much being put into the eye, Harman suggests a "pin" eyedropper. It consists of an ordinary domestic pin fixed into a suitable handle the whole apparatus being chromium plated. The head alone is to be dipped into the oil.

The article is illustrated.

W. ZENTMAYER.

A ROTATING CROSS-CYLINDER. M. TREE, Brit J. Ophth. 23: 632 (Sept.) 1939.

Tree has found that the act of rotating the Jackson crossed cylinder is apt to become an awkward procedure on occasion. He has devised an instrument with a rotating crossed cylinder. The handle is mounted at right angles to a semicircular scale, which is marked in degrees from 0 to 180 as on the ordinary trial frame. The crossed cylinder lens is mounted within the semicircular scale and is rotated in it by means of a cogwheel situated at the upper part of the handle. Directions are given for the manipulation of the instrument.

An illustration accompanies the article.

W. ZENTMAYER.

Lens

TOTAL EXTRACTION OF THE LENS: COMPARISON OF RESULTS IN THE SAME PATIENT WHOSE OTHER EYE WAS OPERATED ON PREVIOUSLY BY CAPSULAR INCISION. L. GENET, Bull. Soc. d'opht. de Paris 51: 48 (Jan.) 1939.

Genet compares the visual results, the patient's reaction to the operation and the observations by the operator in 7 cases in which both eyes had been operated on for cataract. The first operation was done at some previous time by the extracapsular method; the intracapsular technic was used on the second eye. The visual results were fairly uniform and comparable. The patients remarked that the intracapsular method took longer, but this was because of the necessity of akinesia and retrobulbar injection. They appreciated, however, the fact that there was less pain during the iridectomy because of the anesthesia. The operator finds that operation with the newer method takes longer, especially if sutures are used; however, because of added confidence, the intracapsular method is preferred.

L. L. MAYER.

CARBOHYDRATE METABOLISM OF THE LENS IN ACUTE NAPHTHALENE POISONING. H. K. MÜLLER, Arch. f. Ophth. 140: 171 (Feb.) 1939.

In previous experiments the author has shown that in acute naphthalene poisoning of rabbits two features of the lens metabolism are promptly and markedly interfered with, namely, the reduction of vitamin

C present in the fluid around the lens and the dehydrogenation of lactic acid inside the lens. The author now reports a series of experiments designed to throw light on the mechanism of the disturbances in intermediary carbohydrate metabolism which are brought on by naphthalene. These experiments have revealed that in early stages of naphthalene poisoning the breaking-up of phosphoric acid esters and the formation of lactic acid are increased in the lens. The mechanism of naphthalene poisoning may be an interference with the transfer of hydrogen.

P. C. KRONFELD.

Neurology

EARLY BLINDNESS CAUSED BY DIFFUSE CEREBRAL SCLEROSIS. M. CREMER, Klin. Monatsbl. f. Augenh. **101**: 750 (Nov.) 1938.

A boy aged 3 years, whose mind was well developed at the age of 2, showed symptoms of failing vision for three months. The fundi showed no pathologic changes, and the pupils reacted promptly to light; therefore, the source of blindness was located in the cortex of the brain. The Pirquet and Wassermann tests were negative, and the spinal fluid was normal. Paralysis of the legs and tongue were followed by spasms. Contractions of the arms and legs were noted later; the child could swallow only liquid food, and respiratory difficulties developed during the last period of life. Death followed about two years after the first visit. Pathologic examination showed two well defined foci of sclerosis over the second and third ventricles and numerous small foci scattered in the vicinity of these ventricles. The marrow sheaths were destroyed, and finely granular, fatty degeneration was observed in the cortex. This chronic process of sclerosis resembled the type described by Schilder. The diffuse appearance of the process resembled that of disseminated sclerosis. Similar cases reported by other authors are mentioned.

K. L. STOLL.

INDIRECT HETERONYMOUS HEMIANOPIAS: REPORT OF CASES. K. VELHAGEN JR., Klin. Monatsbl. f. Augenh. **101**: 801 (Dec.) 1938.

The author reports detailed histories in 8 cases of increased intracranial pressure, adding charts of the field of vision and roentgenograms of the base of the skull, with especial reference to the chiasm. Velhagen arrived at these conclusions: Bitemporal and binasal defects of the field of vision occur in processes associated with increased intracranial pressure which are not located in the area of the chiasm. The disturbances of the field of vision were indirect and distant symptoms. He discusses the question of how far such disturbances of the field of vision may be caused indirectly by processes in the neighborhood of the chiasm. Especial consideration is given so-called secondary rarefaction of the sella turcica as a consequence of increased intracranial pressure. Hydrocephalus of the third ventricle appears to play a predominant role in such instances. The possibilities of the differential diagnosis between direct and indirect heteronymous hemianopias and direct and indirect lesions of the sella turcica are discussed.

K. L. STOLL.

Ocular Muscles

THE DIAGNOSIS OF PARALYSES AND CONTRACTURES OF MUSCLES FOR VERTICAL OCULAR MOVEMENTS. I. BORSOTTI, Ann. di ottal. e clin. ocul. **67**: 241 (April) 1939.

The author, in an extensive article, describes a scheme for exact diagnosis of paralytic vertical deviations as proposed by Franceschetti. The principles and data of Bielschowsky are employed, but the author considers that Franceschetti's chart eliminates the necessity of the somewhat complex reasoning required for a diagnosis by Bielschowsky's method. On this chart the essential data are first considered, and the data of secondary importance are included for confirmation of the diagnosis. Various pitfalls of the methods commonly employed are considered with the precautions necessary to avoid them. The author considers the use of horizontal objects of especial importance in determining deviation of the images. The test for such inclination with the head in various positions is considered as affording useful auxiliary data. Six cases are described and analyzed by means of data afforded by the chart.

S. R. GIFFORD.

Orbit, Eyeball and Accessory Sinuses

PARALLEL STUDY OF THE PATHOGENESIS OF RHINOGENOUS OPTIC NEURITIS AND OF SEROUS IRITIS. B. WALDMANN, Am. J. Ophth. **22**: 44 (Jan.) 1939.

Waldmann cites several cases of neuritis and iritis, evidently due to sinus infection. He discusses their pathogenesis and gives the following summary:

"As can be seen from the foregoing, the pathogenesis of optic neuritis and of serous iritis displays considerable differences; they have, however, many points in common.

"The optic neuritis of rhinogenic origin is the outcome of an aseptic process going on in the optic canal, and is brought about exclusively by mechanical factors. Its origin is in the empyema of the posterior sinuses, or the chronic hypertrophic inflammation of the latter.

"Spontaneous serous iritis, even in the presence of syphilis or tuberculosis, is in every instance the outcome of a catarrhal infection.

"The source of infection is the catarrhal inflammation of the posterior sinuses, and pathogenic agents migrate directly from the sinus into the canal and thence, by way of the pia mater, into the uvea."

W. S. REESE.

Parasites

CYSTICERCUS IN THE SUBCUTANEOUS FAT OF THE LID. M. ROSENZWEIG, Vestnik oftal. **13**: 270, 1938.

A firm tumor the size of a large bean was found at the lower orbital margin, under the skin of the lid of the left eye of a woman aged 38. She complained of nausea and occasional vomiting. Two years previously she noticed hookworms in the stool. Three years previously she ate pork

which was rejected by the sanitation department. An encapsulated tumor was removed through an incision in the skin; the capsule was opened, and a transparent vesicle came out, inside of which the head of a Cysticercus was found.

O. SITCHEVSKA.

Pharmacology

CHOLINE BODIES AS HYPOTENSIVE COLLYRIA. A. MAGITOT, Bull. Soc. d'opht. de Paris **51**: 38 (Jan.) 1939.

For some years the foreign literature, especially the German literature, has reported new substances used as collyria in the treatment of glaucoma. These products are of the acetylcholine family and are difficult to procure in France. The three important cholines used have been: (1) acetylbetamethylcholine, known in France as hypotan and in the United States as mecholyl (employed as a general hypotensive agent), (2) carbaminoylcholine, known under the name of doryl, and (3) carbaminolymethylcholine, called iricoline. Reid Hunt in 1914 and Villaret, Besançon and Gallois in France in 1931 used a 5 per cent solution of mecholyl but found it inferior to pilocarpine. Velhagen introduced carbaminoylcholine in 1934. Good effects have been reported in the German and Italian medical journals with 2 or 3 per cent solutions. Six case reports are given to show the inconsistency in the results with this drug. Four cases are reported to evaluate the use of carbaminoylmethylcholine. Magitot concludes that the last two drugs are hypotensive medicaments which have the same efficacy in cases of hypertensive glaucoma as does pilocarpine. They are inferior to physostigmine salicylate but are better tolerated.

L. L. MAYER.

Refraction and Accommodation

A CONTACT-LENS-TELESCOPIC SYSTEM. J. W. BETTMAN and G. S. MCNAIR, Am. J. Ophth. **22**: 27 (Jan.) 1939.

Bettman and McNair cite a case and give the following summary of their method of improving vision:

"A method for constructing a telescopic spectacle by using a contact lens with a flat corneal segment as an eyepiece and a strong positive lens in an ordinary spectacle frame as the objective has been described. The patient for whom this contact-lens-telescopic system was prescribed was able to see as well at distance with it as with his Zeiss telescopic lens, and was able to read better. The cosmetic disfigurement was much less than with the Zeiss telescope and the field of vision was not restricted."

W. S. REESE.

Retina and Optic Nerve

SPASM OF THE TRUNK OF THE CENTRAL RETINAL ARTERY. A. HUDELO, Bull. Soc. d'opht. de Paris **51**: 14 (Jan.) 1939.

The case reported here is presented for the following reasons: 1. The spasm was localized in the retrobulbar portion of the artery.

2. Ophthalmoscopic examination of the retinal arteries presented special aspects. 3. Changes caused by direct pressure on the eye could be followed from minute to minute. 4. The sequela of retinitis which followed the spasm could be satisfactorily explained by the previous difficulty. 5. Cranial disturbances were associated with ocular difficulties.

The patient, a man of 39 years, had vertigo and short periods of loss of vision in the lower field of the left eye. Six months later there developed hemiplegia with aphasia of several minutes' duration. One month later diplopia and passing mouches volantes developed. After another month left hemiparesis occurred with a positive Babinski sign. In this episode there was total blindness of the right eye lasting one-half hour. All the vessels of the fundus were exsanguinated. Acetylcholine was injected retrobulbarly at intervals. The light reflex was entirely abolished. Gradually the blood column reappeared in all the vessels and vision increased accordingly over a period of months. There was little modification in the appearance of the retina during the critical period, and no "cherry" spot or local spasms occurred. Pigmentation in the chorioretina appeared, but whether this was present before the acute attack is not known. General and retinal arterial pressures remained within the normal range. Many questions remain unanswered with reference to this interesting case. L. L. MAYER.

CLEAVAGE OF THE RETINA AND VENOUS LESIONS. S. SCHIFF-WERTHEIMER and R. GALAN, Bull. Soc. d'opht. de Paris **51**: 21 (Jan.) 1939.

A woman of 25 years had had sudden loss of vision of the right eye for three weeks. The acuity was reduced to 0.2, the inferior portion of the visual field being lost. In the superior and temporal portions of the retina there was a white tract which divided into two portions, one curving forward into the vitreous and the other extending toward 7 o'clock. The visual acuity remained normal. Various changes were noted in the affected area. The condition appears to be similar to that described by Mary as retinitis proliferans succeeding resorbing hemorrhages. The basis seems to be a fundamental disease of the veins. Two excellent photographs of the fundus are shown. L. L. MAYER.

SYMMETRIC BINOCULAR RELATION OF GROUPS OF RETINAL TEARS TO THE TERMINAL VESSELS: REPORT OF A CASE. O. VOGT, Klin. Monatsbl. f. Augenh. **101**: 861 (Dec.) 1938.

In his book on detachment of the retina, Vogt described the close relation of groups of retinal tears to certain terminal vessels. Nearly all branches of a terminal vessel showed attachments to holes and cysts in the retina, resembling grapes or berries. In the present paper he describes a similar condition in the eyes of an emmetropic woman aged 56. He noted ten holes and tears in the temporal periphery of the left eye, whereas not a single hole could be observed in the nasal periphery, nor was there any suggestion of the formation of a cyst. The arrange-

ment of the holes and cystoid formations in the right eye corresponded to that in the left. Vision was normal in the right eye and nearly so in the left. The holes were closed prophylactically by katholysis and diathermic punctures, although detachment had not yet developed.

K. L. STOLL.

SUBVASCULAR WHITE DOTS IN THE DETACHED RETINA RESEMBLING WHITE PRECIPITATES: REPORT OF A CASE. A. VOGT, Klin. Monatsbl. f. Augenh. **101:** 864 (Dec.) 1938.

Round white dots in the detached retina assumed the arrangement and shape of precipitates on Descemet's membrane in a man aged 30. The dots were most numerous in the intermediary zone and less frequent in the periphery and axially. They were chiefly located subvascularly and were occasionally grouped in plaques, covering the vessels in some instances. The dots disappeared completely after operative treatment of the retinal detachment in this case and in that of 2 women, aged 56 and 60, respectively. The histologic substratum of these spots remains unknown.

K. L. STOLL.

QUESTION OF THE SIGNIFICANCE OF INTACT RETINAL PERIPHERY IN ALBUMINURIC RETINITIS. Y. KOYANAGI, Klin. Monatsbl. f. Augenh. **101:** 884 (Dec.) 1938.

The author disagrees with Volhard's theory that albuminuric retinitis is nothing but malnutrition of the retina caused by angiospastic ischemia. This disease is known to involve almost solely the area of the posterior pole of the eye, including the disk and macula, but to have no tendency to spread into the periphery or to cause concentric contraction of the field of vision. Furthermore, the disease never begins in the periphery.

Koyanagi discusses the different conditions in other retinal and choroidal diseases in which the periphery is involved and in which the field of vision is peripherally contracted. He concludes that the nutritional diseases of the retina, usually associated with a lack of oxygen, may arise in different ways. They may be caused by vascular changes due to disturbances of the circulation of the blood or by inferiority of the circulating blood. Notwithstanding the characteristic changes depending on etiologic factors, these diseases begin in the periphery, as evident by ophthalmoscopic examination and by the concentric contraction of the field of vision. The author goes as far as to maintain that no nutritional diseases of the retina occur without involvement of the periphery. He denies that pale hypertension and ischemic disturbances remain limited to the central area of the retina, even if only certain ramifications of the central artery are spastically contracted. Albuminuric retinitis, therefore, cannot be caused by angiospastic nutritional disturbances, as claimed by Volhard. The retinal center, in the author's opinion, possesses better nutritional facilities, even if angiospastic circulatory disturbances should involve the retinal arteries in pale hypertension.

K. L. STOLL.

Trachoma

TREATMENT OF TRACHOMA WITH SULFANILAMIDE. F. JASSERON and G. MORARD, Bull. Soc. d'opht. de Paris 51: 212 (April) 1939.

In a preliminary study (*Oranie méd.*, December 1938, no. 8, p. 10) the authors reported most favorable results following the oral administration of sulfanilamide to 20 patients with trachoma. Since then about 100 patients treated in this manner have been under observation. In the present report the results obtained by 21 of these patients are described in some detail. The authors' conclusions follow:

1. The subjective symptoms of pain, photophobia and tearing disappeared in forty-eight hours.

2. In 80 per cent of the patients with pannus, regression occurred in eight days.

3. The ulcers of the cornea observed in 16 per cent of the cases epithelized in thirty-six hours.

4. The cicatricial process was greatly accelerated. A change from stage II to stage III occurred in one week, and in two weeks the cicatrization of stage III was found to be far advanced.

5. Complications observed were general urticaria in 2 cases, local urticaria of the face in 1 case and erythema of both hands appearing toward the end of the treatment in 2 cases. With the addition of sodium bicarbonate, most of the complications have not been noted.

6. The dose used varies according to the weight of the patient. As a rule 2 Gm. are given the first five days, 1.5 Gm. the next four days and 1 Gm. the last four days, or a total of 20 Gm. in thirteen days.

The authors are satisfied that this is the best treatment yet discovered.

L. L. MAYER.

Tumors

EPITHELIOMA OF THE CORNEOSCLERAL LIMBUS. C. DEJEAN, H. VIALLEFONT and J. FERRIE, Arch. Soc. d. sc. méd. et biol. de Montpellier 20: 15 (Jan.) 1939.

Examination of a man aged 54 who complained of tearing in the right eye, disclosed a smooth, hard, circumscribed epibulbar formation along the temporal limbus, adherent to the overlying conjunctiva. The tumor was excised, curetted and seared. Histologic study revealed an unruly growth of epithelial cells with many giant nuclei. Though malignant, the tumor rarely penetrates deeply. In another case, that of a man of 72, such a growth had been quiet for twenty-eight years. In the succeeding two years it grew to the size of a dime, involving one third of the limbus and occasioning a constant neuralgia. Six months after enucleation a cancerous nodule appeared in the orbit, so that a subperiosteal orbital exenteration was finally required.

J. E. LEBENSOHN.

EPITHELIOMA OF THE MEIBOMIAN GLAND OF UNUSUAL ASPECT. DOLLFUS, E. JOSEPH, COURTIAL and P. DESVIGNES, Bull. Soc. d'opht. de Paris **50:** 23 (Jan.) 1939.

A man of 46 years had an entropion of the lower left lid which had been present for some three years. In appearance, it was like a millet seed. Ulceration of the area developed, and medical care was of no avail. On surgical removal the lesion showed grossly a degree of caseation which was suggestive of malignancy. Histologic examination revealed a basal cell epithelioma. An external canthotomy was done, and radium was applied to the area of the lesion. The fact that the patient had some knowledge of difficulty with the lid for as long as ten years and that the lesion passed through stages of ulceration and cicatrization without adenopathy was remarkable. The usual radium sensitivity of the lesion and its prompt cure were rather unusual.

L. L. MAYER.

RETINAL GLIOMA WITH SPECIAL CONSIDERATION OF HEREDITY: REPORT OF CASES. H. LANGE, Klin. Monatsbl. f. Augenh. **101:** 854 (Dec.) 1938.

W. Stock, of Tübingen, and K. A. Reiser, of Bonn, reported 28 and 16 cases of glioma of the retina, respectively, in only 1 of which the glioma was undoubtedly of the hereditary type. Other statistics are noted in this paper. Lange reports on 36 cases of retinal glioma observed at the ophthalmic clinic of the University of Halle. He found that none of the children with bilateral glioma could be cured, but died. Glioma may be hereditary, but the reason remains unknown why it is not hereditary in every case. In all cases of bilateral glioma observed at the clinic at Halle the condition was hereditary, a sign that hereditary glioma is especially malignant. Hemmes, observing the same phenomenon in his cases, noted that the glioma was bilateral in children of a parent who had suffered from glioma in one eye. The proportion of patients with glioma compared with those with all other ocular diseases varies between 0.01 and 0.078 per cent according to various authors; according to Lange it was 0.0217 per cent. Thus patients with glioma constitute a very small portion of the population. Hemmes estimates that the incidence of glioma is 1 in every 34,000 living children born in Holland. In closing, Lange states that the information obtained from the families regarding the occurrence of glioma is probably not reliable and that therefore a number of cases will remain unknown.

K. L. STOLL.

Uvea

CHOROIDAL ANGIO-SCLEROSIS WITH SPECIAL REFERENCE TO ITS HEREDITARY CHARACTER. A. SORSBY, Brit. J. Ophth. **23:** 433 (July) 1939.

It would appear that three clinical forms of choroidal sclerosis have been described: (*a*) central senile areolar choroiditis, in which a more or less regular oval area extends from the disk temporally and engulfs the macula; (*b*) the peripapillary type, in which the choroidal sclerosis

radiates from the disk to a variable but considerable extent peripherally in all directions, and (*c*) generalized sclerosis, in some cases of which the macula is spared while in others it is engulfed.

Sorsby reports familial cases of central senile areolar choroidal sclerosis, peripapillary choroidal sclerosis, central and peripapillary choroidal sclerosis and generalized choroidal sclerosis.

The review of the literature and the personal observations establish choroidal sclerosis as a distinct clinical entity of a familial character. Night blindness and undue contraction of the field were not features in any of the cases reported in the present study. The distinction between a peripapillary type and a central peripapillary type of choroidal sclerosis has some justification. There is some validity in the view advocated by Ascher that retinitis pigmentosa shows two forms, one mesodermal, or choroidal, and the other ectodermal, or retinal.

The nature of choroidal sclerosis requires elucidation. The case reported in this article establishes the familial character of the condition and the fact that the lesion develops in adult life. Presumably the choroidal circulation earlier in life was normal. In so far as the lesion appears to develop in postnatal life in fully differentiated tissue and is of a hereditary character, it may be regarded as belonging to the group of heredodegenerations or abiotrophies.

The article contains a number of colored and black and white plates.

W. ZENTMAYER.

LUPUS PERNIO AND PLASTIC IRITIS. J. MARGAROT, P. RIMBAUD and J. RAVOIRE, Arch. Soc. d. sc. méd. et biol. de Montpellier **20**: 53 (Feb.) 1939.

In a woman with a history of tuberculous glands in childhood, a recurrent and progressive plastic iridocyclitis, associated with swelling over the parotid glands and stomatitis, had developed since the age of 21. After 47 she manifested in the winter chilblain-like lesions in the nose, ears, fingers and knees. The tests for tuberculous allergy were negative, which is the usual finding in the Besnier-Boeck-Schaumann syndrome. The authors suggest that both the iritis and the lupus pernio were probably due to sarcoid.

J. E. LEBENSOHN.

Therapeutics

VITAMIN THERAPY IN OPHTHALMIC PRACTICE. J. LAVAL, Am. J. Ophth. **22**: 33 (Jan.) 1939.

Laval discusses vitamins A, B, C and D and their uses in ophthalmology. He gives the following summary:

"It is suggested that in cases of the following vitamin deficiencies it might be theoretically valuable to prescribe the following treatment:

"1. Vitamin A—Prescribe a tablespoonful twice daily in cases of poor dark adaptation, phlyctenular kerato-conjunctivitis, photophobia, and low-grade conjunctivitis in women who are on a slenderizing diet or in cases of other corneal and conjunctival lesions in which the history shows a lack of vitamin-A intake.

"2. Vitamin B (B_1 and B_2)—Prescribe eight yeast tablets daily of the brewers'-yeast type put up by any of the reliable pharmaceutical firms, or the powdered form may be ordered. This is to be used in cases of incipient cataract, in optic neuritis, retrobulbar neuritis, and also in toxic amblyopia.

"3. Vitamin C—Order the juice of at least two large oranges or one grapefruit daily in cases of incipient cataract. (This is plus the brewers'-yeast which is also to be taken daily). In cases of intraocular hemorrhage order the juice of four lemons daily." W. S. REESE.

INTRAOCULAR TENSION IN ELECTROPYREXIA. H. C. ERNSTING, Am. J. Ophth. **22**: 54 (Jan.) 1939.

This is a preliminary report and is mainly a discussion of hyperpyrexia induced by the Kettering cabinet. The electropyrexia seems to lower intraocular tension. W. S. REESE.

Society Transactions

EDITED BY W. L. BENEDICT

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

DAVID H. WEBSTER, *Chairman*

ROBERT K. LAMBERT, M.D., *Secretary*

Nov. 20, 1939

Groenouw's Corneal Dystrophy. DR. WALTER HIPP.

A case of unusual keratitis was reported. The condition could not be definitely classified but was thought to be Groenouw's dystrophy.

Lymphangioma of the Orbit. DR. HERMAN GOLDBERG (by invitation).

A case of lymphangioma of the orbit with conjunctival involvement, which had been present since birth, was reported. Biopsy of the tumor revealed dilated lymphangiomatous tissue. Various methods of therapy were outlined, and the use of sclerosing solutions was thought to be indicated in this case. Twenty-two cases of lymphangioma of the orbit were reviewed.

Congenital Retinal Folds. DR. FREDERICK THEODORE and DR. JOSEPH ZIPORKES.

This paper will be published in full in a later issue of the ARCHIVES.

The Relation of Drusen of the Optic Nerve to Tuberous Sclerosis. DR. ALGERON REESE.

This paper will be published in full, with discussion, in a later issue of the ARCHIVES.

Syphilitic Atrophy of the Optic Nerve and Papilledema Due to Optochiasmal Arachnoiditis: Indications for Surgical Intervention. DR. LOUIS HAUSMAN (from the Neurological Service, Cornell Division, the Bellevue Hospital).

Data on a series of patients are presented to emphasize the need for keeping in mind the occurrence of arachnoid adhesions around the chiasm in cases of syphilis and also to point out the indication for surgical intervention in such cases and the benefits of this approach in the restoration or improvement of vision.

In the neurologic service of Dr. Kennedy at the Bellevue Hospital, I had the opportunity recently of studying 15 patients with syphilitic disorders of the optic nerve. All the patients presented a history of syphilis, or serologic evidence of it, and rapid loss of vision, frequently terminating in blindness. One patient presented papilledema, 1 secondary

atrophy of the optic nerve and the remaining 13 primary atrophy of the optic nerve.

Five of the patients were operated on and of these, 4 had the chiasm explored. The remaining patients either refused operation or are still under observation. Only those persons who were operated on will be discussed. These may be divided into three groups, according to the essential clinical features presented by them.

Group 1.—The characteristic features presented by the patients in this group were bilateral primary atrophy of the optic nerve, heteronymous visual defects or almost total blindness and a normal ventricular system without evidence of internal hydrocephalus. This group consisted of 3 patients, and at operation all showed adhesions around the optic chiasm and nerves. The adhesions were removed. The usual transfrontal approach to the chiasm was employed. After operation, vision improved. The patient in case 1 in this group has now been observed for more than two years. The visual fields and visual acuity in both eyes have continued to improve steadily since the operation. The visual fields in both eyes are greatly expanded. Uncorrected visual acuity in the left eye is 16/15 and in the right eye 16/15 — 2. Color vision also has returned in both eyes. Before operation this patient was blind in the left eye and had temporal hemianopia in the right eye.

Group 2.—The characteristic features presented by this group were secondary atrophy of the optic nerve and internal hydrocephalus. A typical case report (case 4) follows:

The patient gave a history of progressive loss of vision for three years. At one time she had bilateral papilledema. On admission the visual fields showed irregular concentric constriction, partly sector shaped, and bilateral secondary atrophy of the optic nerve. An encephalogram revealed internal hydrocephalus. Operation was not advised because it was felt that the visual disturbances were secondary to the internal hydrocephalus rather than adhesions at the chiasm. However, the patient wished to have the operation, with the hope that at least it would prevent blindness even if it did not improve her vision. Operation was performed, but no unusual adhesions were found at the chiasm. Vision has remained unchanged.

Group 3.—The characteristic features presented by the patients in this group were papilledema without internal hydrocephalus and adhesions around the optic chiasm. A typical case report (case 5) follows:

The patient presented concentric constriction of the visual fields, enlargement of the blindspot, bilateral papilledema and normal spinal fluid pressure. A ventriculogram revealed no internal hydrocephalus but a slight shifting of the ventricular system to the left. A right subtemporal decompression was done; however, the patient did not improve, and her condition steadily became worse. At autopsy the following findings were noted: a syphilitic plastic meningitis around the optic chiasm, a small gumma of the right parietal lobe and no internal hydrocephalus.

In this case, removal of the gumma in the right parietal lobe would probably not have improved visual function, for the impairment was apparently due not to increase in the intracranial pressure but to exudate at the base enveloping and strangling the optic nerves and producing swelling of the disk through some local mechanism.

Summary.—When symptoms are present such as those presented by the patients in group 1, adhesions around the optic chiasm and nerves

should be suspected and the patient treated surgically. For patients such as those in group 2, it would seem that exploration of the chiasm is not indicated. The findings for group 3 would indicate that for this type of patient exploration of the chiasm is warranted.

I realize that this is too small a series on which to base any definite conclusions; for that reason I am merely presenting the facts with the hope that more patients may be studied along these lines in an attempt to evaluate the benefit of the surgical approach which the material thus far suggests.

DISCUSSION

DR. BERNARD SACHS: I am extremely gratified that Dr. Hausman has presented this subject before an ophthalmologic group. It was more than forty years ago that I was intensely interested in syphilis of the brain and particularly in associated basilar symptoms. No one at that time would have dared to attempt operative intervention or even have thought that anything could be gained by such manipulation of the nerves at the base of the brain. Therefore, this report presents not only well worth while data, as Dr. Hausman has shown the excellent results obtained in 2 or 3 cases, but implications of far greater significance than just the record of these few cases. The one thing that impresses me more than anything else is the point that none of the ophthalmologists present would have interfered in a case in which blindness had lasted for a number of years or would have thought that after release of the adhesions function of that nerve could be restored. It is a most hopeful finding, and I think for this reason that the communication deserves special consideration. No doubt many of these patients come to the ophthalmologist more frequently than they seek the neurologist. As a rule, many of them have symptoms pointing to involvement of the various nerves at the base of the brain. Such involvement is common, the third and sixth nerves being most frequently affected. However, in view of Dr. Hausman's report, I see no reason why one should hesitate to think of operative intervention in these cases, even if other nerves are involved.

I doubt whether such cases will become more numerous than they have been. Owing to the improved antisyphilitic treatment and medicinal chemotherapy, postsyphilitic diseases of the central nervous system are growing far less numerous. I only need to call attention to the fact that dementia paralytica is a much rarer disease than it was fifteen years ago. Tabes, Dr. Kennedy stated at a recent meeting of the New York Neurological Society, is becoming so rare that he has difficulty in finding patients to demonstrate the disease before his classes. The improvement in the treatment of arachnoiditis at the base of the brain is undoubtedly satisfactory, but the point which one can well afford to stress is that once the diagnosis is made, particularly of syphilitic chiasmal arachnoiditis, and if the other symptoms warrant intervention, then operation should be attempted as early as possible. The case reported by Dr. Hausman in which the blindness lasted for many years in one eye, the eye did not recover after operation, but the other eye, in which the duration of blindness was much shorter, did recover. While it is surprising that the chiasm stands as much pressure as it seems to, the earlier the surgical intervention, other things being equal, the more satisfactory the result will probably be.

The subject is a promising one. The facts that my own knowledge of arachnoiditis of the base of the brain, and particularly of chiasmal arachnoiditis, was gained largely from postmortem examinations many years ago and that now one has a chance of approaching this condition at the operating table show that a distinct advance has been made in therapy.

DR. THOMAS JOHNSON: To make a diagnosis of arachnoiditis in the cisterna chiasmatica is difficult. The symptoms in arachnoiditis involving the visual pathways are so varied they do not present any definite pattern. Primary and secondary atrophy of the optic nerve and changes in the visual fields are so common in syphilis of the nervous system that it is hard to obtain a clue as to the presence of arachnoiditis. If studies of the visual fields could be made in the early stages of the disease when the pressure on the chiasm might be localized at the crossed fibers, bitemporal hemianopia possibly could be found which would materially aid in making a diagnosis. Treatment early in the disease before too much destruction of the nerve tissues has taken place is desirable.

Hartmann listed the characteristic change in the visual fields as being an irregular concentric contraction with central scotoma.

Cushing stated that the diagnosis of cisternal arachnoiditis was one he was exceedingly loath to make in the absence of postmortem examination.

A diagnosis of syphilitic adhesive arachnoiditis involving the chiasm is justified if there are atrophy of the optic nerve; bitemporal hemianopia or a blind eye with a temporal hemianopia in the fellow eye; absence of bone destruction in the chiasmal area, as shown roentgenographically; absence of an expanding lesion, as shown by encephalographic or ventriculographic examination, and positive serologic findings or other definite clinical evidence or symptoms of syphilis.

The question of whether the improvement in vision justifies such radical treatment suggests itself.

In 1916 Walker and Cushing, in a paper on atrophy of the optic nerve associated with chiasmal lesions, reported 3 cases of interpeduncular cysts in which symptoms and signs of the chiasmal syndrome were present. Cushing evacuated the cysts but apparently did not break up any existing adhesions. The vision of 1 patient was slightly improved, 1 patient became totally blind and the third showed little change in vision. The patients survived the operation two, five and one month, respectively.

Frazier, in a paper on pseudotumors, discussed 22 cases of arachnoiditis. In 11, symptoms of lesions of the posterior fossa were present, and in 11, pretentorial symptoms. The symptoms suggested a pituitary lesion in 4 of the cases and a suprasellar lesion in 1. In 3 of the 5 cases vision improved after operation, and in 2 the elapsed time was too short to say whether or not the vision was improved. The type of operation was not described, but the impression left was that decompression was done with evacuation of pretentorial fluid. No deaths were reported.

Craig and Lillie discussed 8 cases of arachnoiditis in which operation was performed for relief of visual loss. The results were: case 1, no improvement in vision; case 2, relief of headache and two months after operation normal visual fields; case 3, death due to pneumonia on the fifth postoperative day; case 4, death in two days; case 5, death three

days after operation; case 6, no improvement in vision; case 7, slight improvement in vision, and case 8, right nasal hemianopia. In case 8 there was a complete return of the right nasal field after operation.

In 11 of Frazier's cases the structures of the posterior fossa were involved. This brings to mind the rare cases in which the aqueduct of Sylvius becomes obstructed, with resulting extensive enlargement of the third ventricle. After such distention the anterior wall of the ventricle may be pushed forward, simulating a cyst, and press on the chiasm, causing atrophic changes in the optic chiasm and nerves. The destruction is not due to pressure alone but to traction from normal or newly formed fascial bands. Fay and Grant list four structures which, because of their close relationship, may exert pressure on the visual pathways in the presence of large suprasellar lesions. The structures noted are the dural band connecting the anterior clinoid processes, the internal carotid arteries, the anterior cerebral arteries and the anterior communicating artery. I have in mind a boy who presented chiasmal symptoms, with papilledema, and was operated on for a suprasellar cyst. He died of pneumonia after the operation, and an arachnoiditis with a tremendously distended third ventricle was found at autopsy. It was evident that the anterior wall of the third ventricle had compressed the optic chiasm and nerves, causing the visual symptoms.

It does not appear that the patients in the cases mentioned were syphilitic, but they serve, along with those in the cases reported by Dr. Hausman, the purpose of illustrating what visual results may be expected after operation and what may be the mortality risks.

Of course, modern diagnostic methods have been greatly improved, and the present day surgical procedures for the brain are far in advance of those of a few years ago.

In a case of syphilis with progressive loss of vision in which a diagnosis of arachnoiditis involving the optic chiasm and nerves has been made and medical treatment has failed to improve the vision, it would seem that craniotomy with the evacuation of fluid and freeing of adhesive bands is justifiable.

DR. ISADORE GIVNER: I should like to report a case which I think brings out two points. First, the patient has dementia paralytica of the tabetic form, a condition which it is felt is characterized by parenchymatous changes; yet after operation and the release of the adhesions about the optic chiasm, her vision improved. Second, I was able to follow the course of the patient's blindness from the beginning and to see how the field defect progressed up to the time of operation and how it receded after operation.

The patient, who is aged 29, was first seen in October 1938 with a history that two months previously she had been in a hospital with a diagnosis of "acute gastritis." During that time she noticed she had lost the vision in the right eye. When she was first seen she had vision of 10/200 in the right eye and 20/20 in the left eye. On October 29 the field of her left eye with a 3 degree test object at 330 mm. contracted temporally to 70 degrees; the other fields were normal for form; in the right eye there was a contraction nasally for form to 30 degrees. At this stage a left homonymous hemianopia could be demonstrated with a red test object. The fields were next charted on Jan. 4, 1939, at which time that of the left eye showed little change and the right field showed an increase in the nasal constriction.

During this time I had examined her and had obtained a history of rapid loss of vision. The findings included a normal sella turcica, positive Wassermann reactions of the blood and spinal fluid, a colloidal gold curve of the paretic type and a spinal fluid cell count of 9. I felt that the patient had syphilitic arachnoiditis involving the optic chiasm. She was given intense antisyphilitic treatment and heat therapy. She received five heat treatments preoperatively and seven postoperatively. The question arose here as to whether the heat therapy or the operation helped her, but as the condition progressed steadily under the heat therapy and was not helped until operation, the improvement is considered to be due to the latter.

On March 4 the vision in her right eye had become reduced to perception of light and in the left eye to 20/50. On April 3 the vision in the left eye was 20/200 + 1. The field taken on May 25 showed a complete loss of the temporal field of the left eye. Her vision had decreased to 15/200. In this case the operation which Dr. Hausman suggests was not one of choice but of necessity. Here was a young woman who was going blind in spite of everything the syphilologists could do. I was familiar with the operation discussed here from Vail's work, and I suggested that the patient should see a neurosurgeon. Dr. Arthur MacLean advised and performed a transfrontal craniotomy. The operation done on June 2 showed fine weblike adhesions binding the optic chiasm. These were freed, and the cisterna chiasmatica was opened and drained. By June 12 the patient had already improved. The last field, taken on November 16, showed the left temporal field to have enlarged from 0 to 50 degrees. The vision in her left eye is 20/70—. The patient was able to come here this evening by herself.

Bollack, David and Poech in 1937 reviewed 129 cases of surgically proved arachnoiditis. They found that the condition in 13, or 10 per cent of the cases, was syphilitic and that chiasmal adhesions were present in all. In 6 there was no improvement, in 3 the patients became worse, in 2 there was marked improvement, and in 2 but slight improvement after operation. I think that Dr. Hausman's results compare favorably with these statistics.

Dr. Arnold Knapp: I was particularly struck by the fact that the results of the operation appear to be permanent. I should like to ask Dr. Hausman whether the rapidity with which the changes in the visual field take place can be considered an indication for operation. Finally, will Dr. Hausman be good enough to tell of his experience in operations in the cases of tabes?

Dr. Abraham Kaplan: Patients with atrophy of the optic nerve, particularly of syphilitic origin, are likely to seek an ophthalmologist or a syphilologist; it is unusual for them to come to the neurologist.

There have been 5 cases of this nature at the Bellevue Hospital, the 4 included in groups 1 and 2 of Dr. Hausman's series and a fifth, not mentioned, which belongs to the first group. There has not been a single operative fatality in this series. In 4 of the 5 cases there was improvement, and in the case in group 2, as Dr. Hausman pointed out, visual improvement did not occur. The operation used is right transfrontal craniotomy, just as for a pituitary tumor. The dura is opened, and the frontal lobe is elevated, exposing the optic nerves and the chiasm. Curiously enough, in addition to the adhesions, one usually finds large and small locules of fluid in the region of the chiasmal cistern and the

interpeduncular space. It was pointed out by Dr. Kennedy at the meeting of the New York Neurological Society that likely this condition is more or less of a vestige of a syphilitic basilar meningitis; that is, with the early treatment nowadays the other nerves escape the pressure effect of the disease process, whereas the optic nerve and the chiasm are more vulnerable. At operation adhesions are freed and the locules are broken up, allowing for a better circulation of the fluid and thereby relieving the pressure on the optic nerves. It is surprising, indeed, how much pressure these nerves really tolerate. The optic nerves have been found to be small, white and atrophic; sometimes one nerve is definitely much smaller than the other.

The rate of visual loss has not come under my observation, because I have seen the patients in the late stages, but I have had the pleasure of measuring the return of visual acuity and visual fields after operation.

DR. LOUIS HAUSMAN: Dr. Sachs has raised several interesting points, especially with reference to the viability of the optic nerves and the significance of multiple lesions of the cranial nerves in these cases. I, too, have been struck by the viability of the optic nerves. It is amazing how much return of vision can take place in the presence of white optic disks, despite a long-standing history of blindness. In case 1, for example, the patient was blind for two years, and on examination the disks were extremely white. Now more than two years since the operation, visual acuity has returned almost to normal, despite the fact that the optic disks are just as white as they were before the operation. The degree of pallor of the optic disks is no contraindication to operation. Cushing has stressed this point with reference to tumors of the sella turcica pressing on the optic chiasm.

As to the presence of other cranial lesions, it is well to note that such multiplicity makes the diagnosis of arachnoiditis at the base of the brain somewhat easier. In case 1 the olfactory nerves as well as the optic nerves were involved. Such a combination is not due to any parenchymatous disease but either to a tumor or to adhesions at the base of the brain compressing the olfactory and optic nerves. In such cases the function of these parts can be improved only by surgical intervention.

Dr. Sachs states that these cases are becoming less numerous; that may be so, but I should like to call attention to the fact that Berens and Goldberg in a survey of 100,000 cases of blindness found that about 6,000 of the patients presented a history or a clinical picture suggestive of syphilis. Only 37.5 per cent had been given serologic tests, and of these, about 20 per cent had positive reactions. Furthermore, more than 500 of the patients had atrophy of the optic nerve. Of these, only 50 per cent had been given serologic tests, and of this 50 per cent 25 per cent had positive reactions. It may well be that many of these cases belong to group 1 and that the patients might be helped by surgical intervention instead of remaining a burden to the community.

Dr. Johnson has referred to the question of diagnosis and treatment of these patients. Of course, the diagnosis is easier to make when the patients are seen earlier and give evidence of heteronymous visual defects, which are referable to the optic chiasm. It is important, therefore, to take the visual fields early and often in cases of syphilitic atrophy of the optic nerve. Suppose that a patient with primary atrophy of the optic nerve, evidence of syphilis and total blindness, seeks an

ophthalmologist for diagnosis and treatment, and suppose that the ophthalmologist is not entirely certain that the condition is due to adhesions around the optic chiasm; certainly, he is not justified in making the usual diagnosis of tabetic atrophy of the optic nerve in these cases, albeit, this has been the practice of both ophthalmologists and neurologists. Such a diagnosis is, I believe, incorrect, because frequently in these cases there is no evidence of tabes, if by tabes is meant disease of the dorsal roots or dorsal columns, which are nothing more than extensions of the dorsal roots. Furthermore, it is this diagnosis which really has been an obstacle to therapy. It has been misleading to regard the visual defect as evidence only of parenchymatous disease of the optic nerve, for it has precluded the existence of adhesions and thus blocked the surgical approach. The operation itself is not a dangerous one. Of course, any operation on the brain is a serious procedure, but of all of them I think the transfrontal approach offers much less risk, as there are no vital areas in this region; the chiasm is readily accessible. There has been no mortality in this series in which the chiasm was explored. As Dr. Johnson points out, the literature presents some cases in which the results have not been so good. The condition in these cases was not due to syphilis, and the cases are not comparable to those which I have presented, because the disease has not been sufficiently defined. Dr. Johnson refers to cases of internal hydrocephalus due to a lesion of the aqueduct of Sylvius. None of the patients in my series presented such a lesion. The only case of internal hydrocephalus was case 4 in group 2, and in this case the internal hydrocephalus was probably due to exudate at the base of the brain, which obliterated the foramens of Luschka and Magendie and thus prevented a flow of cerebrospinal fluid from the ventricular system into the subarachnoid space. In the lantern slides which I showed I included an encephalogram made in this case. I also pointed out that exploration of the optic chiasm was not indicated but was done at the patient's request, against my advice. To evaluate accurately the cases of chronic nonsyphilitic arachnoiditis reported in the literature, many factors must be taken into consideration, such as the nature of the changes in the optic nerve, the character of the visual defects and the size and shape of the ventricular system. It should be noted also that many successful surgical results have been reported.

With reference to the case of dementia paralytica of the tabetic form, I was interested to note that the visual defect was due to adhesions around the chiasm and was improved by surgical intervention. The point was raised whether heat therapy may have played a part in the restoration of vision in this case. I do not think so, because the vision returned too soon after operation.

Dr. Knapp has raised the question as to the permanence of the results in these cases. In this respect the results obtained in case 1 are significant. The patient has now been observed for three years since the operation. Visual acuity still remains good and the fields expanded. In the cases of visual impairment due to chronic nonsyphilitic arachnoiditis reported by Heuer, he pointed out that not only did the vision improve after liberation of the adhesions around the chiasm but the benefits of the operation persisted. Heuer had occasion to observe these cases for several years.

In cases of syphilitic arachnoiditis of the optic chiasm, the loss of vision is rapid. Many of the patients become totally blind within two years; it is therefore important to watch the progress in these cases carefully, to chart the visual fields frequently and to note the visual acuity on these occasions. When the vision in such cases becomes progressively and rapidly worse, the likelihood of adhesions around the optic chiasm and nerves should be entertained. The presence of tabetic signs, such as absence of knee jerks or ankle jerks, should not deter one from coming to this conclusion. One should remember that in tabes dorsalis adhesions occur around the dorsal roots as part of the pathologic process. It is not difficult to imagine that the same type of lesion may occur around the optic chiasm or that both lesions may exist in the same patient. As a matter of fact, in case 2, in which adhesions were found around the optic chiasm, the ankle jerks could not be elicited.

If a patient has been treated adequately, and despite this treatment the danger of blindness is imminent, he should be informed of the surgical approach. If the physician is in doubt, he should acquaint the patient with all the facts and let him decide for himself whether he wishes to choose the risk of operation or to remain a burden to himself and the community for the rest of his life. I, myself, would encourage the patient to accept the surgical approach, for he would have everything to gain and little to lose.

I was pleased to hear Dr. Kaplan discuss the surgical approach in these cases. He is familiar with this problem, for he has operated in several of the cases which I presented this evening. As he intimated, the approach is not difficult, and of all the operations on the brain it is perhaps the least dangerous. It can be performed with a minimum of risk to the patient's life in skilful hands. Further clinical studies are necessary to determine in what type of case surgical measures should be used. So far, the evidence points strongly to the cases which I have described in group 1 and possibly in group 3.

COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

FRANCIS HEED ADLER, M.D., *Chairman*

WARREN S. REESE, M.D., *Clerk*

Jan. 18, 1940

Corneal Ulcer Associated with Lymphogranuloma Venereum: Report of a Case. DR. GEORGE P. MEYER and DR. JACOB REEBER.

A case of corneal ulcer with unusual features was presented because of the rare association of this condition with lymphogranuloma venereum. The clinical features of lymphogranuloma venereum were briefly discussed, together with the ocular complications reported by other observers. Corneal ulcers have not been reported as a complication of lympho-

granuloma venereum. The ulcer in the case reported responded quickly to the administration of sulfanilamide after other measures had failed to stop its progress. The etiologic relation and specific tests were discussed.

Diseases of the Eye Produced by Viruses. DR. PHILLIPS THYGESON.

This paper will be published in full, with discussion, in a later issue of the ARCHIVES.

Book Reviews

Traité d'ophtalmologie. Published under the auspices of the Société française d'ophtalmologie, by P. Bailliart, C. Coutela, E. Redslob, E. Velter and R. Onfray, general secretary. Eight volumes, pp. 8,058, with 176 plates in color. Subscription, unbound edition, 2,500 francs; bound edition, 2,800 francs. Single volume, 350 or 400 francs. Paris: Masson & Cie, 1939.

Volume V contains 860 pages, 250 figures and 69 plates in color. This volume continues the general subject of special pathology and takes up diseases of the iris, diseases of the ciliary body and diseases of the choroid, by M. Teulières and J. Beauvieux; diseases of the retina, by P. Bailliart; recurring retinal hemorrhages in adolescents, by P. Jean-Delize and P.-L. Drouet; detachment of the retina, by M. Amsler and S. Schiff-Wertheimer; tumors of the retina, by Jacques Mawas; diseases of the disk, by L. Bollack and S. Delthil; tumors of the disk, by Jean Nordmann, and diseases of the lens, by C. Duverger and E. Velter.

It treats, in short, many of the most interesting clinical problems in ophthalmology and presents the views of the French school so successfully as to make it an outstanding volume of the series. One of the important chapters is that by Bailliart on retinal diseases (250 pages), in which the clinical picture is illustrated by excellent drawings of the fundus in color and photographs of the fundus. Splendid reproductions of the histologic changes of the conditions under consideration add greatly to the completeness of the presentation. Another chapter which deserves special comment is the one on retinal detachment, by Amsler and Schiff-Wertheimer (100 pages), which takes up the clinical study, prognosis, indications for operating, etiology and pathogenesis. It is a most scholarly and instructive presentation.

Volume VI, containing 960 pages, 390 figures and 18 plates in color, concludes the subjects of pathology and begins the subject of ocular neurology. The concluding chapters of the section on pathology are entitled: "Diseases of the Vitreous Body," by F.-E. Koby; "Congenital Diseases of the Eyeball," by J. Coppez; "Injuries," by M. Danis; "Burns," by Léon Coppez; "Panophthalmitis and Sympathetic Ophthalmia," by J. Coppez; "Pathologic Intraocular Tension," by A. Magitot; "Diseases of the Orbit," by F. Terrien; "Complications Associated with Disturbances of the Neighboring Organs" and "Craniorbital Malformations," by André Patry; "Disturbances of the Eye in Relation to Ocular Disease," by G. Worms and H. Tillé; "Ocular and Orbital Complications of Sinus Disease" and "Disturbance Secondary to Tonsil and Tooth Infections," by G. Worms.

The important chapter is that on glaucoma (130 pages), which is admirably presented by Magitot, who has supplied so many valuable studies for this difficult subject. An unusual and interesting feature of this volume is a consideration of the diseases of structures adjacent to the orbit.

The second part of the volume is devoted to ocular neurology, and various subjects are treated under the following titles: "Introduction to Ocular Neurology," by Auguste Tournay; "Nontraumatic Diseases of the Optic Nerve" and "Traumatic Disturbance of the Optic Nerve," by Gilbert and Gabriel Sourdille; "Tumors of the Optic Nerve," by Jean Nordmann; "Diseases of the Chiasm," by Edward Hartmann and Marcel David; "Diseases of the Retrochiasmic Optic Pathways and of the Visual Cortex," by A. Monbrun, and "Ophthalmic Migraine" and "Scintillating Scotoma," by Jean Gallois.

The important chapter is the one on the optic nerve (120 pages) in which the following conditions are taken up in turn: tumors of the brain, meningitis (serous and arachnoiditis), infections of the nervous system (multiple sclerosis, myelitis and tabes), toxic amblyopia, autointoxication and diseases of the circulatory system.

An excellent and brief description of the lesions which produce the chiasmic syndrome is contributed by Hartmann and David.

ARNOLD KNAPP.

Ocular Dominance in Relation to Developmental Aphasia. By M. MacMeeken, Department of Psychology, Edinburgh University. Pp. 60. London, University of London Press, 1939.

This short monograph is one of the publications of the W. H. Ross Foundation for the Study of Prevention of Blindness.

MacMeeken concludes from the examination of 383 children 3 years of age that a significant percentage (8 to 10 per cent) of children in the Edinburgh schools are severely handicapped by a language difficulty of specialized pattern—a language disability not only affecting reading but spreading over to affect other language functions. Ocular and auditory defects, changes in school and absences from school are not the causes of these reading difficulties, although they may be contributing factors. MacMeeken holds the prime cause to be a "developmental aphasia."

"A significant relationship was found between disability and left-eyedness as determined by sighting or directional tests of eyedness. Every one of these disability children was found to be left-eyed." A child was considered left eyed if on casually being presented with a paper tube to look through, a 12 inch rule to sight along and a cardboard with a "keyhole" opening to peek through he chose the left eye for the task. There is no account of how many trials were made. This comment is applicable to many of the author's procedures and experimental controls, which are sufficiently vague to validify considerable doubtfulness regarding his conclusions. Some of the typical reading errors he describes can adequately be explained without recourse to the postulate of aphasia and entrance into the highly speculative field of localization of mental functions.

MacMeeken has not proved that ocular difficulties may not be an important factor in the production of reading difficulties. He examined the eyes and ocular muscles of only 36 of the 383 subjects, and the results were not negative in every instance.

MacMeeken seems more hopeful than Orton regarding the possibilities of assisting these children, but remedial methods are referred to only in the section on "Summary and Conclusions" and are not dealt with at all in the investigation.

The author believes something ought to be done about these children and puts the onus on the school authorities and educators. But they certainly do not know what to do, and neither do the psychologists, psychiatrists, neurologists, ophthalmologists nor orthoptists. Perhaps in the last group lies the greatest hope for assistance.

LEGRAND H. HARDY.

A Guide to Ophthalmic Operations. By J. Bruce Hamilton, Hobart, Tasmania. Foreword by Sir William James Barrett, Melbourne, Australia. Price, 10 shillings 6 pence net. Pp. 201. London: H. K. Lewis & Co., Ltd., 1940.

As an adjunct to treatises on the surgery of the eye, Dr. Hamilton's little guide is a welcome addition. It brings the important accessories to the surgical operation which are frequently hard to find listed in a book.

After a description of the preparation of the dressings and of the patient, the care and sterilization of instruments are taken up. Enumeration of the instruments also carries references to a number in the instrument catalogues. Then follow descriptions of the arrangement of the operating room and of the dressing tray, methods of sterilization and the use of drops and solutions; a list of drugs in general use, and, finally, a description of the diet before and after operation.

Each operation in favor in the British ophthalmic hospitals is taken up in turn, with consideration of the medicaments for anesthesia, of instruments and sutures, of the necessary nursing after operation and of the frequency of dressings.

This is a useful book and will be of value not only to the surgeon but to the assistant and nurses in the operating room.

ARNOLD KNAPP.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6°, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6°, France.

International Ophthalmologic Congress

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

International Organization Against Trachoma

President: Dr. A. F. MacCallan, 33 Welbeck St., London, W., England.

FOREIGN

All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

British Medical Association, Section on Ophthalmology

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

Chinese Ophthalmology Society

President: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen, Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.
Place: Heidelberg. Time: Aug. 5-7, 1940.

Hungarian Ophthalmological Society

President: Prof. H. G. Ditroi, Szeged.
Assistant Secretary: Dr. Stephen de Grosz, University Eye Hospital, Maria ucca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secreatry: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

NORTH OF ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. A. MacRae, 6 Jesmond Rd., Newcastle-upon-Tyne, England.
Secretary: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

OPHTHALMOLOGICAL SOCIETY OF AUSTRALIA

President: Dr. A. James Flynn, 135 Macquarie St., Sydney.
Secretary: Dr. D. Williams, 193 Macquarie St., Sydney.
Place: Perth, Western Australia. Time: Sept. 2 and 7, 1940.

OPHTHALMOLOGICAL SOCIETY OF EGYPT

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the Secretary, Dr. Mohammed Khalil.

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

President: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Secretary: Mr. L. H. Savin, 7 Queen St., London, W. 1, England.

OPHTHALMOLOGY SOCIETY OF BOMBAY

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

OXFORD OPHTHALMOLOGICAL CONGRESS

Master: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.
Time: July 4-6, 1940.

PALESTINE OPHTHALMOLOGICAL SOCIETY

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

POLISH OPHTHALMOLOGICAL SOCIETY

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

ROYAL SOCIETY OF MEDICINE, SECTION OF OPHTHALMOLOGY

President: Dr. Malcolm Hepburn, 111 Harley St., London, W. 1, England.
Secretary: Dr. C. Dee Shapland, 15 Devonshire Pl., London, W. 1, England.

SOCIEDADE DE OPHTALMOLOGIA E OTO-RHINO-LARYNGOLOGIA DA BAHIA

President: Dr. Francisco Ferreira, Pitangueiras 15, Brotas, S. Salvador, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

SOCIETÀ OFTALMOLOGICA ITALIANA

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

SOCIETY OF SWEDISH OPHTHALMOLOGISTS

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4 III tr., Stockholm, Sö.

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Secretary: Dr. Derrick T. Vail Jr., 441 Vine St., Cincinnati.
Place: New York. Time: June 10-14, 1940.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President: Dr. Frank E. Brawley, 30 N. Michigan Ave., Chicago.
Executive Secretary-Treasurer: Dr. William P. Wherry, 1500 Medical Arts Bldg., Omaha.
Place: Cleveland. Time: Oct. 6-11, 1940.

AMERICAN OPHTHALMOLOGICAL SOCIETY

President: Dr. Frederick Tooke, 1482 Mountain St., Montreal, Canada.
Secretary-Treasurer: Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn.
Place: Hot Springs, Va. Time: June 3-5, 1940.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

Chairman: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Secretary-Treasurer: Dr. C. S. O'Brien, University Hospital, Iowa City.
Place: New York. Time: June 11, 1940.

CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto.
Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.
Place: Royal York Hotel, Toronto. Time: June 19-21, 1940.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President: Mr. William Fellowes Morgan, 50 W. 50th St., New York.
Secretary: Miss Regina E. Schneider, 50 W. 50th St., New York.
Executive Director: Mrs. Eleanor Brown Merrill, 50 W. 50th St., New York.

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. Andrew Rados, 31 Lincoln Park, Newark.
Secretary: Dr. William F. McKim, 317 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. E. G. Nadeau, 122 E. Walnut St., Green Bay.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.
Place: The Gateway Inn, Land O'Lakes. Time: June 1940.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. Edwin B. Goodall, 101 Bay State Rd., Boston.
Secretary-Treasurer: Dr. Trygve Gundersen, 243 Charles St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. Frederick G. Sprowl, 421 Riverside Ave., Spokane, Wash.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.
Place: Spokane, Wash. Time: June 24-27, 1940.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Clarence W. Shannon, 4th and Pike Bldg., Seattle.
Secretary-Treasurer: Dr. Purman Dorman, 1215–4th Ave., Seattle.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month, except June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. L. A. Shultz, 303 N. Main St., Rockford, Ill.
Secretary-Treasurer: Dr. J. J. Potter, 303 N. Main St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Don M. Howell, Alma, Mich.
Secretary-Treasurer: Dr. Louis D. Gomon, 308 Eddy Bldg., Saginaw, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July and August.

SIOUX VALLEY EYE AND EAR ACADEMY

President: Dr. R. A. Kelly, 304 N. Main St., Mitchell, S. D.
Secretary-Treasurer: Dr. J. C. Decker, 515 Frances Bldg., Sioux City, Iowa.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. Grady E. Clay, Medical Arts Bldg., Atlanta, Ga.
Secretary: Dr. John R. Hume, 921 Canal St., New Orleans.

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President: Dr. Dake Biddle, 123 S. Stone Ave., Tucson, Ariz.
Secretary: Dr. M. P. Spearman, 1001 First National Bank Bldg., El Paso, Texas.

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President: Dr. Carl Wencke, Battle Creek.
Secretary-Treasurer: Dr. A. K. Zinn, Battle Creek.
Time: Third Thursday of alternate months.

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. C. M. Harris, Johnstown.
Secretary-Treasurer: Dr. C. Wearne Beals, 41 N. Brady St., DuBois.

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. Virgil Payne, Pine Bluff.
Secretary-Treasurer: Dr. Raymond C. Cook, 1005 Donaghey Bldg., Little Rock.

COLORADO OPHTHALMOLOGICAL SOCIETY

President: Dr. Melville Black, 424 Metropolitan Bldg., Denver.
Secretary: Dr. John C. Long, 324 Metropolitan Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. Shirley H. Baron, 309 State St., New London.
Secretary-Treasurer: Dr. S. J. Silverberg, 201 Park St., New Haven.

Eye, Ear, Nose and Throat Club of Georgia

President: Dr. Grady E. Clay, 384 Peachtree St. N. E., Atlanta.
Secretary-Treasurer: Dr. J. Mason Baird, 511 Medical Arts Bldg., Atlanta.

Indiana Academy of Ophthalmology and Oto-Laryngology

President: Dr. Marlow W. Manion, 23 E. Ohio St., Indianapolis.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: Indianapolis. Time: First Wednesday in April.

Iowa Academy of Ophthalmology and Oto-Laryngology

President: Dr. H. H. Lamb, American Bank Bldg., Davenport.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.
Place: Davenport.

Louisiana-Mississippi Ophthalmological and Otolaryngological Society

President: Dr. D. C. Montgomery, 301 Washington Ave., Greenville, Miss.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

Michigan State Medical Society, Section of Ophthalmology and Otolaryngology

Chairman: Dr. O. B. McGillicuddy, 124 W. Allegan St., Lansing.
Secretary: Dr. A. R. McKinney, 330 S. Washington Ave., Saginaw.

Minnesota Academy of Ophthalmology and Otolaryngology

President: Dr. Hendrie W. Grant, 330 Lowry Medical Arts Bldg., St. Paul.
Secretary-Treasurer: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Time: Second Friday of each month from October to May.

Montana Academy of Oto-Ophthalmology

President: Dr. Roy Grigg, Bozeman.
Secretary: Dr. A. W. Morse, 507 Phoenix Bldg., Butte.

New Jersey State Medical Society, Section on Ophthalmology, Otology and Rhinolaryngology

Chairman: Dr. James S. Shipman, 542 Cooper St., Camden.
Secretary: Dr. Wright McMillan, 23 Passaic Ave., Passaic.

New York State Medical Society, Eye, Ear, Nose and Throat Section

Chairman: Dr. Chester C. Cott, 333 Linwood Ave., Buffalo.
Secretary: Dr. Searle B. Marlow, 109 S. Warren St., Syracuse.
Place: New York. Time: May 7-8, 1940.

North Carolina Eye, Ear, Nose and Throat Society

President: Dr. A. G. Woodward, 100 S. James St., Goldsboro.
Secretary-Treasurer: Dr. M. R. Gibson, Professional Bldg., Raleigh.

North Dakota Academy of Ophthalmology and Oto-Laryngology

President: Dr. N. A. Youngs, 322 De Mers Ave., Grand Forks.
Secretary-Treasurer: Dr. F. L. Wicks, 516–6th St., Valley City.

Oregon Academy of Ophthalmology and Oto-Laryngology

President: Dr. Paul Bailey, 833 S. W. 11th Ave., Portland.
Secretary-Treasurer: Dr. R. S. Fixott, 1020 S. W. Taylor St., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

Rhode Island Ophthalmological and Otological Society

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

South Carolina Society of Ophthalmology and Otolaryngology

President: Dr. S. B. Fishburne, 1430 Marion St., Columbia.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville.

Tennessee Academy of Ophthalmology and Otolaryngology

President: Dr. J. B. Stanford, 899 Madison Ave., Memphis.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

Texas Ophthalmological and Oto-Laryngological Society

President: Dr. J. W. Ward, 2607½ Lee St., Greenville.
Secretary: Dr. Dan Brannin, Medical Arts Bldg., Dallas.
Place: Fort Worth. Time: December 1940.

Utah Ophthalmological Society

President: Dr. A. E. Callaghan, Boston Bldg., Salt Lake City.
Secretary-Treasurer: Dr. Rowland H. Merrill, 1010 First National Bank Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

Virginia Society of Oto-Laryngology and Ophthalmology

President: Dr. Charles T. St. Clair, 418 Bland St., Bluefield, W. Va.
Secretary-Treasurer: Dr. M. H. Williams, 30½ Franklin Rd. S. W., Roanoke.

West Virginia State Medical Association, Eye, Ear, Nose and Throat Section

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

Akron Academy of Ophthalmology and Otolaryngology

President: Dr. L. E. Brown, Second National Bldg., Akron, Ohio.
Secretary-Treasurer: Dr. C. R. Anderson, 106 S. Main St., Akron, Ohio.
Time: First Monday in January, March, May and November.

Atlanta Eye, Ear, Nose and Throat Society

President: Dr. Arthur G. Fort, 478 Peachtree St. N. E., Atlanta, Ga.
Secretary: Dr. Lester A. Brown, 478 Peachtree St. N. E., Atlanta, Ga.
Place: Grady Hospital. Time: 6:00 p m., second Wednesday of each month from October to May.

Baltimore Medical Society, Section on Ophthalmology

Chairman: Dr. Frank B. Walsh, Wilmer Institute, Johns Hopkins Hospital, Baltimore.
Secretary: Dr. Fred M. Reese, 6 E. Eager St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to May.

Birmingham Eye, Ear, Nose and Throat Club

President: Each member, in alphabetical order.
Secretary: Dr. N. E. Miles, 408 Medical Arts Bldg., Birmingham, Ala.
Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

Brooklyn Ophthalmological Society

President: Dr. E. Clifford Place, 59 Livingston St., Brooklyn.
Secretary-Treasurer: Dr. Frank Mallon, 1135 Park Pl., Brooklyn.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

Buffalo Ophthalmologic Club

President: Dr. James G. Fowler, 412 Linwood Ave., Buffalo.
Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.
Time: Second Thursday of each month.

Chattanooga Society of Ophthalmology and Otolaryngology

President: Each member, in alphabetical order.
Secretary: Dr. A. H. Benz, 706 Medical Arts Bldg., Chattanooga, Tenn.
Place: Mountain City Club. Time: Second Thursday of each month from September to May.

Chicago Ophthalmological Society

President: Dr. Georgiana Dvorak-Theobald, 715 Lake St., Oak Park, Ill.
Secretary-Treasurer: Dr. Earle B. Fowler, 55 E. Washington St., Chicago.
Place: Medinah Michigan Avenue Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

Cincinnati Ophthalmic Club

Chairman: Each member, in rotation.
Secretary-Treasurer: Dr. E. R. Thomas, 819 Carew Tower, Cincinnati.
Place: Holmes Memorial Library, Cincinnati General Hospital. Time: 8:15 p. m., third Monday of each month except June, July and August.

Cleveland Ophthalmologic Club

Chairman: Dr. Albert J. Ruedemann, Cleveland Clinic, Cleveland.
Secretary: Dr. B. J. Wolpaw, 2323 Prospect Ave., Cleveland.
Time: Second Tuesday in October, December, February and April.

College of Physicians, Philadelphia, Section on Ophthalmology

Chairman: Dr. Alexander G. Fewell, 1924 Pine St., Philadelphia.
Clerk: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

Columbus Ophthalmological and Oto-Laryngological Society

Chairman: Dr. Harry M. Sage, 9 Buttles Ave., Columbus, Ohio.
Secretary-Treasurer: Dr. Hugh C. Thompson, 289 E. State St., Columbus, Ohio.
Place: The Neil House. Time: 6 p. m., first Monday of each month.

Corpus Christi Eye, Ear, Nose and Throat Society

Chairman: Dr. F. K. Stroud, 416 Chaparral St., Corpus Christi, Texas.
Secretary: Dr. Arthur Padilla, 414 Medical Professional Bldg., Corpus Christi, Texas.
Time: Second Friday of each month from October to May.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. Dan Brannin, Medical Arts Bldg., Dallas, Texas.
Secretary: Dr. L. E. Darrough, 4105 Live Oak St., Dallas, Tex.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. E. G. Linn, 604 Locust St., Des Moines, Iowa.
Secretary-Treasurer: Dr. Grace Doane, 614 Bankers Trust Bldg., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.
Secretary: Dr. Arthur S. Hale, 1609 Eaton Tower, Detroit.
Time: 6:30 p. m., first Wednesday of each month.

Detroit Ophthalmological Society

President: Dr. Parker Heath, 1553 Woodward Ave., Detroit.
Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.
Place: Club rooms of Wayne County Medical Society. Time: Third Thursday of each month from November to April, inclusive.

Eastern New York Eye, Ear, Nose and Throat Association

President: Dr. L. A. Hulsebosch, 191 Glen St., Glen Falls.
Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. R. A. Gough, 602 W. 10th St., Fort Worth, Texas.
Secretary-Treasurer: Dr. Charles R. Lees, 806 Medical Arts Bldg., Fort Worth, Texas.
Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Grand Rapids Eye, Ear, Nose and Throat Society

President: Dr. Dewey R. Heetderks, 405 Medical Arts Bldg., Grand Rapids, Mich.
Secretary-Treasurer: Dr. Robert G. Laird, 116 E. Fulton St., Grand Rapids, Mich.
Place: Various local hospitals. Time: Third Thursday of alternating months, September to May.

Houston Academy of Medicine, Eye, Ear, Nose and Throat Section

President: Dr. J. Charles Dickson, 1617 Medical Arts Bldg., Houston, Texas.
Secretary: Dr. William J. Snow, 708 Medical Arts Bldg., Houston, Texas.
Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmological and Otolaryngological Society

President: Dr. C. W. Rutherford, 23 E. Ohio St., Indianapolis.
Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to June.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. E. N. Robertson, Concordia, Kan.
Secretary: Dr. John S. Knight, 1103 Grand Ave., Kansas City, Mo.
Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. Paul Southgate, 117 E. 8th St., Long Beach, Calif.
Secretary-Treasurer: Dr. Kirt G. Parks, 605 Professional Bldg., Long Beach, Calif.
Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. John P. Lordan, 2007 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Colby Hall, 1136 W. 6th St., Los Angeles.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

Louisville Eye and Ear Society

President: Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.
Secretary-Treasurer: Dr. J. W. Fish, Brown Bldg., Louisville, Ky.
Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. Earle Breeding, 1801 I St. N. W., Washington.
Secretary: Dr. Elmer Shepherd, 1606–20th St. N. W., Washington.
Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member, in alphabetical order.
Secretary: Dr. Sam H. Sonders, Medical Arts Bldg., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month.

Milwaukee Oto-Ophthalmic Society

President: Dr. John B. Hitz, 411 E. Mason St., Milwaukee.
Secretary-Treasurer: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.
Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

Montgomery County Medical Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.
Secretray: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. Guy Maness, 119–7th Ave., Nashville, Tenn.
Secretary-Treasurer: Dr. Andrew Hollabaugh, Doctors Bldg., Nashville, Tenn.
Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May.

New Haven Ophthalmological Society

President: Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn.
Secretary: Dr. Frederick A. Wies, 255 Bradley St., New Haven, Conn.

New Orleans Ophthalmological and Otolaryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.
Secretary: Dr. Mercer G. Lynch, Maison Blanche Bldg., New Orleans.
Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to June.

New York Academy of Medicine, Section of Ophthalmology

Chairman: Dr. David H. Webster, 140 E. 54th St., New York.
Secretary: Dr. Robert K. Lambert, 10 101–15th Ave., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

New York Society for Clinical Ophthalmology

President: Dr. Arthur M. Yudkin, 257 Church St., New Haven, Conn.
Secretary: Dr. Benjamin Esterman, 515 Park Ave., New York.
Place: Squibb Hall, 745–5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive.

Omaha and Council Bluffs Ophthalmological and Oto-Laryngological Society

President: Dr. J. T. Maxwell, 1140 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m., dinner; 7 p. m., program; third Wednesday of each month from October to May.

Passaic-Bergen Ophthalmological Club

President. Dr. R. N. Berke, 430 Union St., Hackensack, N. J.
Secretary-Treasurer: Dr. T. A. Sanfacon, 340 Park Ave., Paterson, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

Philadelphia County Medical Society, Eye Section

Chairman: Dr. Walter I. Lillie, 255 S. 17th St., Philadelphia.
Secretary: Dr. Edmund B. Spaeth, 1930 Chestnut St., Philadelphia.
Time: First Thursday of each month from October to May.

Pittsburgh Ophthalmological Society

President: Dr. Adolph Krebs, 509 Liberty Ave., Pittsburgh.
Secretary: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

Richmond Ophthalmological and Oto-Laryngological Society

President: Dr. Rudolph Thomason, Professional Bldg., Richmond, Va.
Secretary: Dr. Richard W. Vaughan, Medical Arts Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

Rochester Eye, Ear, Nose and Throat Society

President: Dr. Edwin S. Ingersoll, 26 S. Goodman St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.
Place: Rochester Academy of Medicine, 1441 East Ave. Time: 8 p. m., second Wednesday of each month from September to May.

St. Louis Ophthalmic Society

President: Dr. J. F. Hardesty, Missouri Theatre Bldg., St. Louis.
Secretary: Dr. Carl C. Beisbarth, 3720 Washington Blvd., St. Louis.
Place: Oscar Johnson Institute. Time: Clinical meeting 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

San Antonio Ophthalmolo-Oto-Laryngological Society

President: Dr. Oscar H. Judkins, 414 Navarro St., San Antonio, Texas.
Secretary-Treasurer: Dr. Wilfred E. Muldoon, 414 Navarro St., San Antonio, Texas.
Place: Bexar County Medical Library. Time: 8 p. m., first Tuesday of each month from October to May.

San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Matthew Hosmer, 384 Post St., San Francisco.
Secretary: Dr. Fred Boyle, 490 Post St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

Shreveport Eye, Ear, Nose and Throat Society

President: Dr. I. Henry Smith, Slattery Bldg., Shreveport, La.
Secretary-Treasurer: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. Walter W. Henderson, 407 Riverside Ave., Spokane, Wash.
Secretary: Dr. Robert L. Pohl, 407 Riverside Ave., Spokane, Wash.
Place: Paulsen Medical and Dental Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. James F. Cahill, 428 S. Salina St., Syracuse, N. Y.
Secretary-Treasurer: Dr. I. Herbert Katz, 713 E. Genesee St., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

Toledo Eye, Ear, Nose and Throat Society

Chairman: Dr. S. H. Patterson, 1251–15th St., Toledo, Ohio.
Secretary: Dr. J. E. Minns, 316 Michigan St., Toledo, Ohio.
Place: Toledo Club. Time: Each month except June, July and August.

Toronto Academy of Medicine, Section of Ophthalmology

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.
Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

Washington, D. C., Ophthalmological Society

President: Dr. Frank Costenbader, 1726 I St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. L. Connor Moss, 1710 Rhode Island Ave. N. W., Washington, D. C.
Place: Episcopal Eye and Ear Hospital. Time: 7:30 p. m., first Monday in November, January, March and April.

Wilkes-Barre Ophthalmological Society

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday of each month from October to May.